A STUDY OF METABOLISM IN SEVERE DIABETES

BY

FRANCIS G. BENEDICT AND ELLIOTT P. JOSLIN

WASHINGTON, D. C.

PUBLISHED BY THE CARNEGIE INSTITUTION OF WASHINGTON

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PREFACE.

The researches in this book are an amplification of the investigation on the metabolism of diabetes mellitus instituted in this laboratory in 1908. The experimental evidence has reached such a point that certain fundamental questions can be adequately discussed; many others are still in the process of investigation.

The complicated nature of calorimetric experiments, the urine analyses, and the respiration experiments have made this study possible only through the active and hearty cooperation of our associates. Most of the respiration and calorimeter experiments were made either by Mr. Thorne M. Carpenter or Mr. L. E. Emmes. The urinary analyses were made in part in the Nutrition Laboratory and in part in the private laboratory of one of us (E. P. J.), with frequent determinations in both places as controls. As before, the determinations of β-oxybutyric acid were made by Dr. F. H. Stanwood in the Laboratory of Biological Chemistry of the Harvard Medical School. The routine clinical urinary examinations were made by Miss Elsie Newman, while the total nitrogen determinations and the sugar determinations by the copper-reduction method were made in the Nutrition Laboratory by Miss Alice Johnson and Miss E. B. Babcock.

For the determinations of the "retention of alkali" by the kidneys in the case of a normal individual studied in connection with this report we are indebted to Dr. Gerald Blake.

Nutrition Laboratory of the Carnegie Institution of Washington,
Boston, Mass., June 14, 1912.

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PART I.

INTRODUCTION.

It is acknowledged by all clinicians that the most satisfactory treatment of diabetes mellitus is obtained by a careful and intelligent regulation of the diet. The use of drugs has invariably met with but transitory success; modern clinicians are therefore relying less and less upon such remedies and are turning their attention more definitely toward a careful dietetic régime. Accordingly it is of fundamental importance that all the knowledge possible should be carefully accumulated regarding the uses made by the diabetic patient of the diet, the demands of the body for nutriment, and the best kinds of food to be ingested. It is of further importance that the reaction of the healthy individual to the narrow diet of the diabetic should be investigated, and this especially because the studies upon acidosis have shown that the metabolism of health may be made to closely approximate that of disease by simple external influences, such as the withdrawal of all carbohydrate and the excessive administration of fat.

In our earlier investigation[1] we endeavored to study the energy transformations of diabetics without giving particular attention to the influence of the intake of food. It was believed that the energy transformations without food should first be clearly established, and then a study should be made of the influence of various foods upon the metabolism of diabetics, with particular reference to the effect of the so-called "oatmeal cure," which has received much attention in recent years.

Although the method of study has not been materially modified in our later observations now to be recorded, our experience in the first series has enabled us to plan to better advantage each individual experiment with the purpose of making it an improvement upon those preceding. Careful attention to experimental details, a most scrupulous regulation of the diet, and the technical experience acquired in the last three years in numerous experiments of this type with both normal and pathological individuals have all helped to raise somewhat the standard of accuracy and give us increased confidence in the correctness of the plan of procedure. In the earlier investigation as many individuals as possible were studied in order to determine their general energy requirement for comparison with the energy requirement of normal individuals; in the later series of observations the attempt was made to study systematically and completely the individual subjects rather than to make a large number of less detailed observations on a variety of subjects. At least three of the cases reported herewith have been most carefully studied over a considerable period of time.

[1] Benedict and Joslin, Metabolism in Diabetes Mellitus, Carnegie Institution of Washington Publication No. 136, 1910.

The fundamentally vital conclusion of our first report, *i. e.*, that the metabolism of diabetics was increased above normal somewhat over 15 per cent, was not readily accepted, as was, perhaps, natural, and criticisms of the methods, particularly of the method of comparison of diabetics with normals, were freely made. While we believe that the earlier results showed definitely that our conclusion was well founded, the fact that the criticisms raised were made by a number of excellent workers in the field of metabolism justified our continuing the accumulation of experimental evidence. As a result of this later work, we find ample confirmation of the conclusion drawn from our earlier investigations, namely, that the metabolism of diabetics was increased (about 15 per cent) above normal. The criticisms raised by a number of writers with regard to this general thesis are discussed in Part III.

In our first report the principal subjects considered were the energy transformations and gaseous exchange of diabetics. Incidentally evidence was presented regarding the dextrose-nitrogen ratio and the ingestion of food. In discussing the influence of the ingestion of beefsteak upon the metabolism of one of the subjects we were entirely at fault in our statements regarding the dextrose-nitrogen ratio—an error that has been clearly pointed out by Lusk.[1]

On the other hand, we see no reason to alter our opinion there expressed that with diabetics the dextrose-nitrogen ratio is at best a very uncertain factor, and unless a rigidly strict carbohydrate-free diet be adhered to for several days, the dextrose-nitrogen ratios have little, if any, significance. Neither do we see any reason for changing our belief that the adherence to a strictly carbohydrate-free diet in severe diabetes during a period of several days is a procedure very much to be questioned. This being the case, the significance of the dextrose-nitrogen ratio for diagnostic purposes has not, we believe, the importance that has been ascribed to it by other writers.

PLAN OF RESEARCH.

The original plan of research involved the study of a number of different problems. Of these, the first was the accumulation of further evidence with regard to the increase in metabolism noted with practically all of the diabetics previously studied. The difficulty incidental to a satisfactory comparison of diabetics with normal subjects was pointed out in great detail in the first report, and while we firmly believe that the evidence there set forth showed that on the average there was an increase in metabolism of 15 per cent in diabetes over health, nevertheless plausible arguments could be brought forward indicating that the comparison of diabetics with normal subjects might not be scientifically sound or correct. The disproportion between the body-weight and the body-surface of the two classes of subjects, the differences in the kinds of food eaten, the possibility of a larger protein katabolism with diabetics, and the error of drawing deductions from one individual as normal and another individual as a diabetic are by no means convincing arguments against our thesis;

[1]Lusk, Science, **33**, p. 433.

nevertheless they remain as possible and plausible criticisms of the conclusion drawn from our earlier work. The later experiments were therefore planned further to clarify the situation and to remove cause for criticism.

It also became necessary to secure additional data with regard to normal individuals. During the progress of this investigation a large number of normal subjects have been studied in connection with the respiration researches in this laboratory, and hence the data are continually increasing. They will here be presented in abstract to show normal metabolism under conditions of experimentation similar to those used with the diabetics studied.

Furthermore, a study of the influence of the ingestion of carbohydrates upon the metabolism of diabetics was deemed of great importance. The early investigations of Nehring and Schmoll,[1] Magnus-Levy,[2] and Leo[3] indicated that with the ingestion of carbohydrates there was frequently no increase in the respiratory quotient. Similarly there was apparently no great increase in the sugar excreted in the urine; at least the increase was not sufficient to offset the excess carbohydrate ingested; and while there may have been a positive carbohydrate balance on that particular day, the respiratory exchange did not indicate a combustion of carbohydrates, since it was not materially higher than during fasting. This presented an anomalous situation in that while carbohydrate was ingested in large amounts, it apparently was neither burned nor excreted, and the question therefore immediately arose as to where this carbohydrate had disappeared. For the purpose of throwing light upon the problem a number of experiments were made in this laboratory in which various carbohydrates were ingested, chiefly levulose and oatmeal, the latter being used particularly on account of the great interest in the so-called "oatmeal cure" for diabetes. Under these conditions the metabolism was studied very exactly in short periods following the ingestion of various amounts of carbohydrates in order to determine whether there was an increase in the metabolism or a variation in the respiratory quotient which would indicate a difference in the character of the metabolism as the time progressed. In this way it was hoped that some light would be thrown upon the character of the metabolism and the apparent storage of carbohydrate.

In at least one or two of the earlier experiments we found an apparently abnormal reaction to the ingestion of protein. With normal individuals the ingestion of protein, particularly in the form of beefsteak, shortly produces a rise in metabolism, *i. e.*, the "specific dynamic action" of the protein. With one of the cases previously reported (Case A) this rise in metabolism did not appear; it was therefore suggested that possibly when the body was extremely glycogen-poor the non-nitrogenous portion of the protein molecule split off when the steak was ingested and was deposited as glycogen instead of being burned, and that the specific dynamic action of the protein might be due to the rapid combustion of the non-nitrogenous parts of the protein molecule. It

[1]Nehring and Schmoll, Zeitschr. f. klin. Med., 1897, **31**, p. 59.
[2]Magnus-Levy, Zeitschr. f. klin. Med., 1905, **56**, p. 86.
[3]Leo, Zeitschr. f. klin. Med., 1891, p. 101.

seemed important to verify this observation, if possible, by further evidence; hence a number of experiments are here included in which beefsteak was ingested.

Our earlier experiments also suggested that during severe acidosis, when the patients were clinically in the worst condition, there was a higher metabolism. The relationship between the acidosis and metabolism was by no means clearly established or, indeed, recognized in our earlier report, but as these investigations progressed, it became desirable to make a particular study of the relationship between the degree of acidosis and the total metabolism. This has been given a special and prominent part in the later research, and the relationship between the degree of acidosis and the total metabolism has proved to be one of the most interesting points in this study.

It was possible so to adjust the diet of the diabetics as to secure with the same subject degrees of acidosis varying from very severe to very light; hence we have here an opportunity of comparing the metabolism of a diabetic with a severe acidosis with his metabolism when without an acidosis. This has proved to be a great advantage, since the results obtained are more strictly comparable than those obtained when comparing the metabolism of a diabetic with a severe acidosis with that of a normal subject without acidosis.

The general plan of the research as outlined in the preceding pages was that upon which the year's work was based, but it became clear as time went on that the program must be so restricted as to settle absolutely one or two fundamentally important points rather than to attempt to secure conclusive evidence on so many different phases of the question as are here outlined. While it was thoroughly practicable to secure evidence with regard to the increased metabolism during different degrees of severity of diabetes, and while the relationship between the severity of diabetes and the metabolism began to be strikingly apparent, nevertheless, for experiments on the ingestion of oatmeal, carbohydrates, and beefsteak, both a certain type of case and a certain type of experimental plan were necessary. For this reason it was more difficult to secure patients for this series of experiments than for a study of the general and broader questions; hence, while a considerable amount of data has been accumulated on the points here raised, we do not presume in this report to discuss in any way the questions with regard to the influence of the ingestion of food, the dextrose-nitrogen ratio, the influence of the ingestion of carbohydrates and sugars upon the positive carbohydrate balance, and similar questions, except in a very general way incidental only to their effect upon the question of the relation between the severity of the diabetes and the general metabolism. On the other hand, it seems desirable to present in this report all of the statistical data for the experiments thus far made, so as to make them available for clinicians and for scientists interested in metabolism during diabetes. A complete discussion of the data, together with additional material, will be given in a subsequent publication.

Consequently the final plan of work considered in this report will be first, the evidence with regard to the increased metabolism during diabetes; second,

the relationship between the severity of diabetes and the degree of increased metabolism; and third, the influence of a carbohydrate-free diet upon the total metabolism of normal individuals. Incidentally the accumulated data justify the discussion of the factors affecting body-weight. In connection with the research a modified method for the rapid quantitative determination of sugar in the urine has been elaborated which is described at some length.

APPARATUS AND METHODS.

The apparatus and methods used in the conduct of this research are essentially those described in the earlier publication.[1] The bed calorimeter has been more extensively employed than has the chair calorimeter, the latter being used for only three experiments in this connection. On the other hand, the respiration apparatus, which has continually undergone minor modifications in methods of technique and facility of operation, though not in principle, has been extensively used.[2] In most instances it has been found that observations made with this apparatus are fully as valuable and essentially the same as are the more time-consuming and expensive observations with the respiration calorimeter; hence we have no doubt of the wisdom or propriety of computing the energy transformations from the gaseous metabolism as determined on the respiration apparatus. The respiration apparatus has the special advantage in that with it experiments can be made rapidly, and thus the time relations of the metabolism, particularly after the ingestion of food, can be more exactly and rapidly studied than in experiments with the respiration calorimeter, with the longer periods of 45 minutes.

DETERMINATION OF GASEOUS TENSIONS OF ALVEOLAR AIR.

Owing to the interesting observations of Beddard, Pembrey and Spriggs,[3] it seemed advisable in certain instances to determine the composition of the alveolar air in severe cases of diabetes. Accordingly, with three subjects (I, N, and Q) observations were made of the carbon-dioxide tension, and at times the oxygen tension, of the alveolar air, these being in large part carried out through the kindness of Mr. H. L. Higgins, of the laboratory staff, who used the Haldane gas-analysis apparatus[4] and both the Haldane and the Plesch methods for determining the alveolar air.[5]

VENTILATION OF THE LUNGS.

Using an Elster meter of the type employed by Zuntz, and a pair of Zuntz valves, the ventilation of the lungs per minute was also occasionally determined with one of the subjects (N).

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[1]Benedict and Joslin, *loc. cit.*, p. 15.

[2]A detailed description of the apparatus, showing its use and technique, has just been published in the Deutsch. Archiv. f. klin. Med., 1912, **107**, p. 156.

[3]Beddard, Pembrey and Spriggs, Proc. Physiol. Soc., Journ. Physiol., 1908, **37**, p. 39.

[4]Haldane, Methods of air analysis, London, 1912.

[5]Haldane and Priestley, Journ. Physiol., 1905, **32**, p. 225; Plesch, Zeitschr. f. Exp. Pathol. u. Ther. 1909, **6**, p. 380.

DETERMINATION OF SUGAR IN THE URINE.

General dissatisfaction with the methods commonly used for the estimation of reducing sugars was expressed in our first report and it was there pointed out that the newly-introduced Citron method, while of value from the clinical standpoint, was of little value from the standpoint of exact scientific research. In our new experiments the Citron method was used for only the earlier determinations of sugar. Those made in the private laboratory of E. P. J. were for the most part carried out by a method suggested by Dr. Stanley R. Benedict,[1] of the Cornell University Medical College. For the more recent analyses, especially those made in connection with the best experiments, a highly improved method was used which was devised by Dr. A. W Peters, of the Nutrition Laboratory. After a most careful study of the conditions affecting reduction, temperature conditions, and concentration, Dr. Peters developed a method using the old Fehling or Allihn solution of copper sulphate and the alkaline tartrate, and has determined the amount of unreduced copper remaining in the solution by a titrimetric method. By this means the most accurate determinations of sugar are possible, this being without doubt the most exact method of sugar determination that has thus far been devised. While the method may be readily used in hospital laboratories, it will probably never be acceptable for private practice. Inasmuch as it represents the most scientific attempt to study quantitatively the method of sugar reduction, it is given herewith in considerable detail. For this presentation of the method we are indebted to its author, Dr. A. W. Peters.

A COPPER-REDUCTION METHOD OF SUGAR ANALYSIS (A. W. PETERS).

The construction of this method of sugar analysis is based upon preceding developments for (1) the accurate volumetric determination of copper in alkaline tartrate liquids; (2) the standardization of the heating power used; and (3) the determination of constant and controllable conditions for the reduction. For more detail reference must be made to the original descriptions.[2] When the apparatus and reagents have once been prepared a single determination occupies from 12 to 15 minutes.

The Heating Power.

A heating apparatus should be set up of such power that it will heat 60 c.c. of distilled water under described conditions through the temperature interval of 35° to 95° C. in 120 seconds ± 5 seconds. The water is placed in an Erlenmeyer flask of the best Jena glass, with a capacity of about 200 cm. and a basal diameter of about 6 cm., so that the depth of the liquid will be about 18 mm. The flask is partially closed with a two-hole stopper, one hole of which

[1] Dr. S. R. Benedict's method is based upon the reducing action of sugars upon an alkaline sulphocyanate solution of copper. See Benedict, Journ. Biol. Chem., 1911, **9**, p. 57.

[2] Peters, Amos W., The sources of error and the electrolytic standardization of the iodide method of copper analysis, Journ. Am. Chem. Soc., 1912, **34**, pp. 422; and A critical study of sugar analysis by copper-reduction methods, Journ. Am. Chem. Soc., 1912, **34**, p. 928.

carries a thermometer. The thermometer should not have a greater error at the boiling-point of water than $\pm 0.5°$ C. when the barometric pressure is taken into consideration. The lower end of the thermometer should be placed at a distance of about 2 mm. from the bottom of the flask and the region of the stem above 35° C. should extend above the upper surface of the stopper so as to be plainly visible. This flask should be placed in the center of a plate of unperforated asbestos gauze carried by a ring-stand so that it can be raised or lowered. The distance between the burner and the asbestos should always fall within the limits of 3 to 5 cm., thus avoiding a long flame which would be easily affected by air-currents. Room-temperature and freedom from drafts should prevail. If the latter condition can not be provided the heating apparatus may be wholly or partially protected by a cylindrical hood of sheet metal or asbestos. The flask as above described containing 60 c.c. of distilled water is placed on the asbestos and the time observed that is required for the mercury to rise from 35° to 95° C. The rough adjustment to 120 seconds is made by regulating the flow of gas so as to change the power of the flame with the position of the asbestos constant at 4 cm. The finer adjustment is made by moving the asbestos plate toward or away from the burner within the limits of 3 to 5 cm. The conditions are not properly adjusted until repeated determinations of the time give constant results within limits of error of only a few seconds. At 120 seconds the standard heating power here adopted has been established.

The Process of Reduction.

The reduction mixtures should be placed in the same kind of flasks, with the same stopper, thermometer, etc., and with the same conditions of heating power as were used for the standardization of the latter. The volume of the reduction mixture is always 60 c.c. It consists of 20 c.c. of Allihn's alkaline tartrate solution plus 20 c.c. of Fehling's copper sulphate solution plus 20 c.c. of distilled water for a blank determination, or, in the case of sugar analysis, of an aqueous sugar solution with enough distilled water added to make a final volume of 60 c.c.

The Fehling-Soxhlet solution contains 34.639 grams of pure crystallized copper sulphate in a volume of 500 c.c., but the purity of the copper sulphate is more important than its exact weight. Since its correct copper content can not with reliability be deduced from the formula $CuSO_4.5H_2O$, this value is found by means of standardized thiosulphate as described on page 11 for the "basis titration." The Allihn alkaline tartrate solution contains 173 grams of sodium-potassium tartrate (Rochelle salt) and 125 grams of potassium hydroxide in a volume of 500 c.c.

For a determination of sugar the flask containing the reduction mixture is placed on the heating apparatus and the time is observed, but in this case the reckoning begins only when the thermometer reaches 95° C. The flask should stand undisturbed in the center of the asbestos gauze until the expiration of 20 seconds after the temperature of 95° C. has been reached. It is then promptly removed, with the stopper and thermometer still in place, and twirled for a few

seconds under the tap in order to cool the mixture rapidly, but only to a few degrees under the boiling-point, since the mixture is to be filtered hot without delay.

A Gooch crucible should have been previously prepared with a very heavy filter, so that suction will draw water through it only slowly. A very close and satisfactory filter may be made by placing a layer of pure talcum powder between two layers of asbestos in the Gooch crucible. A good filter may also be made by substituting for the crucible a calcium-chloride drying-tube carried by a one-hole rubber stopper. This is packed first with glass-wool and upon this is made, in the bulb of the tube, a very heavy mat of asbestos, which may also be made as close as desired by means of talcum. The same filter is used many times, the precipitate being removed from it by nitric acid (original specific gravity of 1.42) which has been diluted with one-half of its volume of distilled water. This requires less time than making a new filter for each determination. The suction-flask should have a capacity of about 200 c.c., so that a titration on the filtrate can be performed in the suction-flask, thus avoiding a transfer of the liquid. Not more than 15 to 20 c.c. of wash-water should be used, as it all remains as part of the final volume at the end of titration. This volume should not exceed 120 c.c., to which volume the concentration of the reagents used for the determination of copper has been adjusted. For the inexperienced it is recommended to make a rough measurement of the final volume of the liquid obtained at the end of titration.

The Determination of Reduced Copper.

The amount of copper that has been reduced under the above conditions is a quantitative index of the amount of sugar originally present. The reduced copper may be determined directly upon the precipitated cuprous oxide or residually by the determination of the amount of copper still remaining unreduced in the alkaline filtrate. The amount of copper in the filtrate may be determined either electrolytically for control or volumetrically by the iodide method. For rapidity combined with accuracy the iodide method is recommended, but only when it has first been controlled for the conditions under which it is to be used. For the alkaline tartrate copper solutions which are here used (*i. e.*, Allihn's alkaline tartrate, etc.) this control has been satisfactorily made. The residual method for the determination of the reduced copper may therefore be regarded as certainly the most rapid as well as accurate when the iodide method is applied as described in the previous references and under the following provisions:

(1) The thiosulphate solution should have a value between 12.5 and 13 mg. of copper per cubic centimeter. It should be standardized preferably against the same stock solution of copper which is to be used in the sugar analyses, and the true copper value of this solution should be determined electrolytically. If, however, the stock solution is made of chemically pure copper sulphate there will be no appreciable difference between the standard value of the thiosulphate determined by this electrolytically controlled solution, and the value obtained by the nitric-acid-talcum procedure above referred to, using

pure metallic copper, which procedure may then be substituted for electrolytic determination on the stock solution. The standardization may appropriately be made on 20 c.c. of the stock solution, which is the same volume as will be used in sugar determinations, and with a final volume at the end of titration in no case exceeding 120 c.c. This volume should contain 20 c.c. of concentrated acetic acid and about 7 c.c. of saturated solution of pure potassium iodide. The thiosulphate value of 20 c.c. of the stock solution of copper sulphate determined in simple acetic-acid solution is designated as the "basis titration," and is of fundamental importance for subsequently testing the constancy of solutions and of conditions even when it is not used for the purpose of standardization. A solution of pure copper sulphate will remain at a constant standard value, but the thiosulphate will change somewhat if much exposed to air and especially to light.

(2) The alkaline filtrates from sugar determinations, whose volume must not exceed 75 c.c., should be acidified with concentrated sulphuric acid. The amount of acid used should be such that the thiosulphate value of a blank determination, in which the unheated reduction mixture of 60 c.c. previously described contains all the reagents but no sugar, will be identical with the "basis titration." This amount has been found by experiment, as described in the previous references, to be 4 c.c. of concentrated sulphuric acid, but should be verified or changed if necessary.

After the mixture has been acidified and cooled to 20° C., potassium iodide is added to the amount of 6 to 7 c.c. of an aqueous solution that is saturated at room-temperature. The iodine which is evolved is titrated at once with thiosulphate, using a solution of soluble starch as an indicator near the close of the titration. The end point should be determined by the "spot test," especially in the presence of urinary or other coloring matter, and may be verified by immediate back titration with a drop of iodine solution of about the same concentration as the thiosulphate.

(3) For the residual method a blank determination is always necessary. The assumption that there is no self-reduction of reagents may lead to error, although by the present method pure and especially freshly prepared reagents show a negligibly small self-reduction. The blank value is obtained with the reduction mixture of 60 c.c. previously described but without the presence of sugar. This is heated and filtered and treated in all respects as when a determination of sugar is made. From the thiosulphate value of the copper thus found unreduced is subtracted the value found in the same way in a subsequent sugar analysis. This thiosulphate difference evidently shows the amount of reduced copper due to the action of the sugar. The difference may be converted into milligrams of copper by means of the standard value of the thiosulphate previously obtained, and the corresponding amount of sugar may be found from a table of reduction values.

The Control of All of the Conditions.

All of the conditions of this method and the technique of the operator can be controlled by the use of a standard solution of pure dextrose. The results

thus obtained are a standard of comparison to determine whether in a given case the conditions have been correctly adjusted for the use of the values for dextrose which are recorded in table 1. From these controls the values for 50 and 100 mg. obtained from a 0.5 per cent or 1 per cent standard solution of pure dextrose were usually selected for the first tests. The quantities to be compared should be the $\frac{\text{Dextrose}}{\text{Copper}}$ ratios, as the limits of error of these are evident from the table.

TABLE 1.—*Reduction values for dextrose.*

I. Dextrose.	II. Copper.	III. Dextrose-copper ratio.[1]	I. Dextrose.	II. Copper.	III. Dextrose-copper ratio.[1]
mg.	*mg.*		*mg.*	*mg.*	
1	1.2±0.13	0.833	60	115.5	0.520
2	2.8±0.1	.714	70	134.4	.521
5	8.2±0.14	.610	80	152.9	.523
8	13.8±0.1	.580	90	171.0	.514
10	17.4±0.3	.575	100	191.6±0.35	.522
15	27.7±0.5	.542	110	208.9±0.15	.527
20	37.1±0.2	.539	120	228.1	.526
25	48.1±0.4	.520	135	255.0	.529
30	57.3±0.05	.524	150	280.8±0.6	.534
35	67.6±0.13	.518	165	306.8	.538
40	76.2±0.1	.525	180	330.5±0.1	.545
45	86.0±0.1	.523	200	349.6	.572
50	96.0±0.5	.521			

[1]Average factor between 48 and 192 mg. copper, 0.522.

This abbreviated table is to be used by means of its $\frac{\text{Dextrose}}{\text{Copper}}$ ratios, which are factors for converting the reduced copper to its corresponding amount of dextrose. The most important property of these ratios from a practical standpoint is that they change their value slowly in comparison with the amounts of reduced copper to which they pertain. For amounts of reduced copper between 48 and 192 mg. no table is necessary, as the ratios fluctuate about a mean common factor of 0.522. In all other regions of the table it should be observed that the slow change of the ratios will enable the operator to interpolate mentally the required ratio for any amount of reduced copper lying between two adjacent values of column II. For the very small amounts of dextrose the third decimal place has no practical significance.

CALORIMETRIC MEASUREMENTS.

It is a matter of much regret and no little chagrin that during the greater part of the time the new experiments on diabetics were being carried out the results obtained with the bed calorimeter were vitiated by some then unknown factor, so that the accuracy of the heat measurement in about two-thirds of the experiments is seriously questioned. In about one-third of the experiments we know the results to be satisfactory and accurate, but we have discarded all of the data rather than select arbitrarily one-third of the material for presentation.

The index of this inaccuracy is to be found in abnormal relations between the carbon-dioxide production, the oxygen consumption, and the heat produc-

tion. As has been pointed out in the earlier report,[1] the relationship between the oxygen consumption and calories and the carbon-dioxide production and calories was a relatively constant one for diabetics, that is, approximately 3.3 calories for every gram of oxygen consumed or carbon dioxide produced. On the completion of the later experiments it was ascertained that these ratios were abnormally low, both for oxygen and for carbon dioxide, while the respiratory quotients as finally determined were in full accordance with the earlier work. A further examination of the results, together with a series of control experiments, showed that the apparatus measured the heat radiated from the body most accurately, and the error was finally found to be in the determination of the water-vapor. It was just at this time that fundamental alterations in the method of determining the water-vapor were being introduced, and unquestionably the errors in heat measurement can be directly ascribed to this. Under these conditions, therefore, we deem it inexpedient to discuss in this report the heat as measured, but as all of the control experiments point toward the highest degree of accuracy in the measurement of the carbon dioxide and oxygen, we can confidently base our discussion upon these two factors. Since in an earlier publication the relationships between oxygen consumption, carbon-dioxide production, and heat production were so thoroughly studied, and since these well-known relationships play an important rôle in so-called "indirect calorimetry," the data for the gaseous exchange in this new series of experiments have an increased significance.

[1]Benedict and Joslin, *loc. cit.*, p. 219.

PART II.

STATISTICS OF EXPERIMENTS ON THE METABOLISM OF DIABETICS.

These experiments were all made with patients from the private practice of one of us. Frequently the patients were placed in the New England Deaconess Hospital, within a short distance of the laboratory, and the diet strictly controlled. Others lived in or near Boston and made periodic visits to the laboratory for experimental purposes.

CLASSIFICATION OF CASES.

The cases were divided into groups with particular reference to severe, moderately severe, and light diabetes. The basis for this classification has been essentially that outlined in our previous publication, namely, under severe diabetes were classed all those who failed to become sugar-free, even though all carbohydrates except the green vegetables were excluded from the diet, or those who became temporarily sugar-free upon vegetable days which were followed by a low quantity of protein in the diet. The cases in this group invariably showed a minus carbohydrate balance when the diet was considerably restricted. The second criterion for determining the severity of the case was the presence of an acidosis. Under moderately severe diabetes were classed those who became sugar-free and showed a positive carbohydrate balance, or with whom the acidosis was either very slight or absent. Only one case of light diabetes was included in the study. This was a fat man, Case M, who

Table 2.—*Description of cases used in the studies on diabetes.*

No. of case.	Designation of case.	Sex.	Age at onset.	Onset.	Present condition.	Duration.	
						yrs.	*mos.*
220	A	M.	39	Gradual, 1900	Died, Aug. 24, 1910	10	.
283	B	F.	39	Gradual, Dec. 1908	Died, coma, Apr. 13, 1910	1	4
246	C	M.	28	Acute, Sept. 1908	Died, coma, Dec. 8, 1909	1	3
319	D	M.	31	Mar. 1909	Died, coma, Jan. 13, 1910	.	10
373	E	M.	17	Sept. 1907	Died, coma, Oct. 13, 1909	2	1
201	F	M.	22	Jan. 1908	Died, pneumonia (?), Feb. 1910	2	1
235	G	M.	31	Transitory glycosuria, Jan. 1901; final onset, Jan. 1905	Died, coma, May 4, 1910	9 or 5	4 or 4
310	H	F.	17	1889	Died, coma, May 3, 1910	21	
295	I	M.	13	1900	Died, May 1912	12	..
289	J	M.	18	Feb. 1908	Died, Sept. 17, 1912	4	7
210	K	M.	44	Nov. 1907	Died, coma, Nov. 4, 1910	3	..
226	**L**	**M.**	**21**	**July 1908**	**Active work, Nov. 11, 1912**	**4**	**4**
177	**M**	**M.**	**47**	**1900**	**Active work, Nov. 11, 1912**	**12**	..
281	N	M.	12	July 1909	Died, coma, Feb. 16, 1911	1	7
194	O	F.	13	Feb. 1908	Died, coma, Dec. 10, 1910	2	10
441	P	M.	16	Dec. 1910	Died, coma, Nov. 5, 1911	..	11
371	Q	M.	13	Sept. 1909	Died, coma, Mar. 14, 1911	1	6
344	R	M.	40	Nov. 1903	Died, pulmonary tuberculosis, Mar. 14, 1912	8	4
336	S	M.	46	1899	Died, coma, Oct. 19, 1910	11	..
381	T	M	41	Sept. 1908	Died, coma, Mar. 5, 1911	2	6
332	U	F.	35	Apr. 1909	Died, coma, Aug. 11, 1911	2	4
320	V	M.	35	July 1909	Died, Feb. 6, 1911	1	7
333	**W**	**F.**	**16**	**Nov. 1908**	**Comfortable, Nov. 11, 1912**	**4**	..
317	**X**	**M.**	**32**	**July 1908**	**Comfortable, May 8, 1912**	**3**	**10**

was able to assimilate at least 100 grams of carbohydrate per day. The number of cases of moderately severe and light diabetes are so few as to make them a secondary consideration in this discussion. A brief description of the cases is given in table 2.

DIET.

The diet of the patient was arranged in accordance with that described in the previous report.[1] By strict diet is meant foods containing no carbohydrates such as meat, fish, eggs, and their derivatives, oil, butter, coffee, and tea. The vegetables used contained varying amounts of carbohydrates, ranging between 5 and 10 per cent; but the total amount of carbohydrates given during the day in the form of cooked and uncooked vegetables closely approximated and is estimated at 10 grams.

LIST OF EXPERIMENTS WITH DIABETICS.

The experimental data from which the deductions in this book are drawn were obtained from a large number of cases with a considerable number of experiments. A list of the experiments in the second series, together with the number of periods, is given in table 3.

TABLE 3.—*List of experiments with diabetics lying in bed, 1910–1911.*

Case	Calorimeter.				Respiration apparatus.			
	Without food.		With food.		Without food		With food.	
	No. of experiments.	No. of periods.	No. of experiments.	No. of periods.	No. of experiments.	No. of periods.	No. of experiments.	No. of periods.
A	...	...		...	1	3	...	...
H	1	3	...	...	...	...	...	...
I	1	2	...	...	...	...	...	...
K		...	...	...	3	7	...	...
L		...	...	...	1	3	1	3
M	1	3	...	...	1	4	...	...
N	7	21	1	3	...	...	1	1
O	...	...	...	...	3	6	2	8
P	1	6	2	6	5	14	6	27
Q	2	6	2	6	...	...	...	...
R	1	2	...	...	...	...	3	4
S	...	...	...	...	1	3	1	4
T	2	4	...	...	...	...	...	...
U	2	6	1	4	4	10	7	31
V	...	...	...	...	1	5		...
W	...	...	...	...	2	7	...	...
X	[1]3	[1]9	...	...	1	3	...	...
Total.	21	62	6	19	23	65	21	78

[1] These experiments with Case X were made with the subject sitting in the chair calorimeter.

As an indication of the amount of experimental material available for deductions, a summarized list of all our experiments to date is also given in table 4.

[1] Benedict and Joslin, *loc. cit.*, p. 29.

TABLE 4.—*Experiments with diabetics, 1908–1911.*

	1908–1910 (13 cases).		1910–1911 (17 cases).		1908–1911 (24 cases).[1]	
	No. of experiments.	No. of periods.	No. of experiments.	No. of periods.	No. of experiments.	No. of periods.
Subjects sitting in chair calorimeter:						
Without food	30	106	3	9	33	115
With food	14	45		..	14	45
Subjects lying in bed calorimeter:						
Without food	11	37	18	53	29	90
With food	..	..	6	19	6	19
Respiration apparatus (lying):						
Without food	26	102	23	65	49	167
With food	..	...	21	78	21	78

[1]Experiments with six of these cases are reported both in this publication and in Publication No. 136.

CASE A.

DESCRIPTION OF THE CASE.

Male; born May 2, 1860; single; traveling salesman; developed diabetes in 1900; came under our observation in October 1908; died August 24, 1910. Full details regarding the history of this case and its treatment previous to 1910 may be found in an earlier publication.[1]

Later history of the case.—During the winter of 1909–10 the patient was in a comfortable condition, and on March 1, 1910 felt quite well. He reported at this time that he had been able to work and that his friends considered that he looked better than he had for two years. The quantity of urine varied from 2.5 to 3 liters. His diet contained approximately 60 grams of carbohydrate, with 8 grams of sodium bicarbonate. In June 1910 abscesses developed in the right ear, and later a furuncle in the occipital region. In the latter part of July there was considerable edema of the right ankle, but this decreased when the sodium bicarbonate was discontinued in the early part of August. In this month the diet was relaxed considerably, the patient eating cantaloupe and watermelon at noon and peaches at night. Constipation was a troublesome symptom, but the strength was fairly good. A physical examination made August 5 showed a weight of 48.6 kilos. without clothes; temperature, 99.1° F.; blood-pressure, 150; pulse-rate, 108; heart of normal size and free from murmurs; liver not enlarged; pupils equal and reacting to light; knee-jerks normal; moderate edema of the ankles. In the upper right chest a few râles could be heard extending down to about the fourth interspace. There was also a slight cough. Later, August 8, 1910, the findings in the chest were confirmed. The patient was last seen on August 22, 1910, soon after his return from a visit in the country, during which he had suffered from gastric indigestion. As a result of this he had ceased eating, omitted the sodium bicarbonate, and symptoms of coma appeared, as was evident from his report of difficult breathing upon August 20. He was slightly more comfortable on August 22, but air-hunger was manifest. At this time the pulse-rate was 100, the temperature normal; the acetone odor was absent from the breath. The patient died on August 24, 1910.

Urine data.—Only a few observations were made of the urine, and unfortunately these are not of great significance, as the patient's diet was not under

[1]Benedict and Joslin, Metabolism in diabetes mellitus, Carnegie Institution of Washington Publication No. 136, 1910, p. 36.

control. August 4–5, 1910, the specific gravity was 1.024, with diacetic acid present, 0.11 per cent of ammonia, 0.36 per cent of nitrogen, and 2.8 per cent of sugar by copper reduction and 2 per cent by rotation. August 9–10, 1910, the total amount of urine was 1625 c.c. with 5.64 grams of nitrogen and 64.3 grams of sugar. August 10–11, 1910, the total amount of urine was 1380 c.c., with a slight trace of albumen, and 3 per cent (41 grams) of sugar. Diacetic acid was also present. The reaction was acid in all instances. The acidosis at this time was far less than during most of the year 1909, and much of October and November 1908. The decrease in sugar and in ammonia may bear a relation to the development of active tuberculosis in the lungs. Case R is, however, a more striking example of this feature.

EXPERIMENTS WITH CASE A.

In the previous publication, 16 calorimeter experiments were reported with this subject. In all but one of these the chair calorimeter was used. The only experiment with the subject reported here is a respiration experiment. The vital statistics are as follows:

Date of birth, May 2, 1860; height, 171 cm.; body-weight without clothing during experiment, 46.1 kilos.

Respiration Experiment No. A1.

Date, August 10, 1910. Body-weight without clothing, 46.1 kilos.

The subject came to the laboratory the morning of the experiment, fasting, and lay down upon the couch at $8^h\ 05^m$ a. m. The experiment began at $8^h\ 26^m$ a. m., continuing for three periods, 11 to 15 minutes in length, with intermissions of 15 and 20 minutes. The experiment was without incident. The results are given in table 5.

Table 5.—*Results of respiration experiment No. A1.*

Date and time.	Duration.	Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration rate.
Aug. 10, 1910:	*min. sec.*	*c.c.*	*c.c.*			
$8^h\ 26^m$ a.m....	10 47	136	. .	. .	71	13
8 52 a.m.....	13 49	133	189	0.71	68	13
9 26 a.m.....	15 7	131	187	.70	68	13
Average	....	[1] 133	[1] 188	.71	69	13

[1] Carbon dioxide eliminated per kilogram per minute, 2.89 c.c.; oxygen absorbed per kilogram per minute, 4.08 c.c.

CASE B.

DESCRIPTION OF THE CASE.

Female; born September 9, 1869; married; doing her own housework; first recognized symptoms of diabetes mellitus at the age of 39, December 25, 1908; came under our observation September 1909; died in coma April 13, 1910.

The earlier history of this case, with the results of experiments made with her, has previously been published.[1] No further metabolism experiments have been made with this subject. The patient gradually failed during the spring of 1910. Her weight on leaving the hospital March 3, 1910, was 40.7

[1] Benedict and Joslin, *loc. cit.*, p. 61.

kilos., without clothes. During the latter part of March she was troubled with indigestion for which her physician gave calomel, and a sore mouth resulted. She continued to lose flesh, had considerable distress from food, with anorexia and sleepiness. April 1, 1910, moderate jaundice developed, and she died in coma upon April 13, 1910. Death was preceded by a convulsion, which was followed by hemiplegia. The urine was not examined after March 1, 1910.

CASE G.

DESCRIPTION OF THE CASE.

Male; born December 1874; married; broker; sugar in urine, January 3, 1901; came under our observation February 13, 1909, but the case had previously been closely studied for many years; died in coma May 4, 1910.

Full details regarding the history of the case and the results of the three calorimeter experiments made with him have been given in the earlier publication.[1] No new experiments were made with this subject. During the successive 15 months he gradually failed, despite an increase of carbohydrates in his diet up to 100 grams and large doses of sodium bicarbonate. The urine remained acid in reaction until death. Albumen was present on May 2, 1910. The urinary record is given in table 6.

TABLE 6.—*Clinical chart—Case G.*

Date.	Volume of urine.	Specific gravity.	Nitrogen	Ammonia. Total.	Ammonia. $\frac{NH_3-N}{Total\ N}$	Sugar by copper reduction.	Carbohydrates in diet.	Carbohydrate balance.	Sodium bicarbonate.	Body weight without clothing.
1909.	*c.c.*		*gms.*	*gms.*	*p. ct.*	*gms.*	*gms.*	*gms.*	*gms.*	*kilos.*
Apr. 5.....	5900	1027	18 1	2.6	11 8	183	103	−80	45	59 5
Oct. 23.....	5190	1027	20 0	3.4	14 0	151	10±	...	45	58 0
1910.										
May 2.....	6260	1019	23 8	5 2	18 0	157	...	...	75	(1)

[1]Weight without clothing, Apr. 20, 1910, 53.1 kilos.

CASE H.

DESCRIPTION OF THE CASE.

Female; born May 19, 1872; single; nurse; developed diabetes at 17 years of age; sugar found in urine at 20 years of age; came under our observation January 17, 1910; died in coma May 3, 1910. The details of the history of this case may be found in the earlier publication previously referred to.[2]

Later history of the case.—During the spring of 1910 the patient continued her occupation as superintendent of nurses of a large out-patient department for tuberculosis. Fair health and strength were maintained. On March 25 the patient had a body-weight of 54.5 kilos., and was reported as being better than she had been for years. On April 11 an examination showed that the lungs were normal, but the patient was suffering from pains in the legs. The urine was pale in color, acid in reaction, and with a very slight trace of albumen. The urinary record is given in table 7.

The patient suddenly decided to go to Europe and would not be dissuaded. On the first day out, as rough weather was encountered, she became seasick, and for the next three days was unable to take food; thereupon coma developed and death ensued May 3, 1910. Attention is called to the similar period of starvation preceding coma which took place in Case A. It would

[1]Benedict and Joslin, *loc. cit.* p. 111. [2]Benedict and Joslin, *loc. cit.*, p. 118.

appear that whenever the store of available carbohydrates in the body is exhausted, coma develops. For this reason carefully instructed diabetic patients are cautioned to guard against sudden inroads upon their scanty store of glycogen by increasing the quantity of carbohydrates in their diet whenever signs of indisposition appear. These patients, Case A and especially Case H, knew this rule, but they were unable to retain any food.

TABLE 7.—*Clinical chart—Case H.*

Date.	Volume of urine.	Specific gravity.	Diacetic acid.	Nitrogen.	Sugar. By copper reduction.	Sugar. By rotation.	Carbohydrate in diet.
1910.	*c.c.*			*gms.*	*gms.*	*gms.*	*gms.*
Mar. 22-23.	3600		+		....	130	....
24-25 [1]....	3900	1023	+	15.2	140	140	100±
Apr. 10-11	3420	1024	+	10.7	135	123	....
21-22	2970		....	12.6	104		....
22 [2]	860		....	2.7	26		....

[1]Ammonia, 3.1 gms.; $\frac{NH_3-N}{\text{Total N}}$ =16.8 per cent.; $NaHCO_3$ taken, 4 to 8 gms. [2]From 7 a.m. to 1 p.m.

EXPERIMENTS WITH CASE H.

Five calorimeter experiments and one respiration experiment with this subject were reported in the previous publication. One experiment with the bed calorimeter is reported here. The vital statistics were as follows:

Date of birth, May 19, 1872; height, 159 cm.; body-weight without clothing during experiment, 54.1 kilos.

TABLE 8.—*Measurements of metabolism.—Calorimeter experiment No. H1.*

Date and period.	Carbon dioxide eliminated. Total.	Carbon dioxide eliminated. Per minute.	Oxygen absorbed. Total	Oxygen absorbed. Per minute.	Respiratory quotient	Average pulse-rate.	Average respiration rate.
Apr. 22, 1910:	*gms.*	*c.c.*	*gms.*	*c.c.*			
[1]9h 23m a.m. to 10h 23m a.m...	18.6	158	17.2	201	0.79	87	23
10 23 a.m. 11 23 a.m...	20.0	170	19.6	228	.74	85	23
11 23 a.m. 12 29 p.m...	20.8	161	20.3	215	.75	86	23
Total, 3 hrs. 6 mins.[2]........	59.4	163	57.1	215	0.76	86	23

[1]Subject drank a cup of black coffee at 7 a.m.
[2]Carbon dioxide eliminated per kilogram per minute, 3.01 c.c.; oxygen absorbed per kilogram per minute, 3.97 c.c. The urine collected between 7 a. m. and 1 p. m. amounted to 860 c.c. and contained 2.73 grams of nitrogen and 25.6 grams of sugar. Sublingual body-temperature at beginning, 98.4° F.; at end 98.2° F.

CALORIMETER EXPERIMENT NO. H1.

Date, April 22, 1910. Body-weight without clothing, 54.1 kilos.

On the day of the experiment the subject ate no breakfast before coming to the laboratory, taking only a cupful of black coffee at 7 a. m. Her evening meal the day before, which was taken at 7 o'clock, consisted of shad with roe, one French roll, and Romaine salad with French dressing. At 10 p. m. the same day she took one-half pint of heavy cream and 4 ounces of wine.

She reached the laboratory at $8^h 03^m$ a. m., and entered the bed calorimeter at $8^h 26^m$ a. m. The experiment began at $9^h 23^m$ a. m., continuing for three 1-hour periods, the last period being extended 6 minutes in order to secure favorable temperature conditions. The experiment ended at $12^h 29^m$ p. m. After

the experiment the subject said that throughout the whole experimental period there was a great pressure on the bladder. This doubtless was the cause of the uneasiness shown by the subject as indicated by the calorimeter temperature fluctuations. The measurements of the metabolism and data regarding the pulse and respiration rates and urine are given in table 8.

CASE I.

DESCRIPTION OF THE CASE.

Male; born February 2, 1886; married; chauffeur; date of onset not known, but probably some time in 1900; sugar found in urine May 1902, with indications that it had been present for some time; came under our observation October 25, 1909; died May 1912. The earlier details of the case have previously been published in full.[1]

An attack of influenza in the spring of 1910 reduced the strength of the patient materially, yet he recovered sufficiently to go into the poultry business

TABLE 9.—*Clinical chart—Case I.*

Date.	Volume of urine.	Specific gravity.	Diacetic acid.	β-oxy-butyric acid.	Nitrogen.	Ammonia. Total	Ammonia. $\frac{NH_3-N}{Total\ N}$	Sugar by rotation.	Carbohydrates in diet.	Carbohydrate balance. (6)	$NaHCO_3$	Body-weight without clothes.
1911.	*c.c.*			*gms.*	*gms.*	*gms.*	*p. ct.*	*gms.*	*gms.*	*gms.*	*gms.*	*kilos.*
Feb. 17–18.	870±	1035	0	..	.	.	.	[1]16.4	.	.		.
18–19.	900±	1038	+	.		.	. .	[1]16.4	215±	. .	0	. . .
19–20..	2220	1036	0		..	.	. . .	[2]147	210	[4]+ 60	0	.
20–21..	1950	1035	0	.	....	. .	....	[2]133	230	[4]+ 95	0	. .
21–22 .	2160	1035	Sl.+	4.5	10.6	1.6	12 4	143	185	+ 40	0	. .
22–23..	2070	1035	Sl.+	5 9	11.4	. . .	.	128	180	+ 50	0	
23–24.	**2555**	**1036**	.	**4 8**	**13 6**	**2.2**	**13 3**	**164**	**175**	**+ 10**	**0**	**40 0**
24–25.	1630	1037	0	3.8	8 3	. . .	. . .	117	155	+ 40	0	
Oct. 2– 3..	6000	1038	0	.	25 8	2.2	7 0	[3]420	..	..		
1912.												
Feb. 9–10..	[5]2040	1036	0	.	....	. .	....	139	175±	+ 35	12	39 4
10–11.	2745	1032	++++	. .	...	1 4	. ..	154	200±	+ 45	12	39 3
11–12..	3150	1030	+++++	.	14 8		....	158	200±	+ 40	12	.
12–13..	2910	1028	+++++	. .	13.4	. .	. ..	116	200±	+ 85	12	
13–14..	2010+	1026	+++++	..	9 6	1 3+	11.1	76	200±	+125	12	.
14–15..	1320	....	.. .	. .	....	...	. ..	.	200±	. .	4	.

[1]Per cent. [2]Sugar by fermentation, Feb. 19–20, 151 gms.; Feb. 20–21, 135 gms. [3]By Fehling's method, 480 gms.
[4]Calculated from fermentation record.
[5]Sediment showed fine and coarse granular casts. Quantities of urine inaccurate, as patient had so many involuntary stools.
[6]The data regarding the urine for this subject can not be considered reliable, as it was impossible to make a careful collection, owing to diarrhea. If such collection had been made, it is probable that this subject would have shown a minus carbohydrate balance, as he did in the period covered by data published in the first report (Publication No. 136, p. 127).

and care for some 70 hens. His diet was not limited and included, among other articles, 2 quarts of milk, 6 oranges, and 10 eggs daily. In February 1911, he returned to the hospital on account of diarrhea which had existed for some time. Under hospital care the number of stools decreased from 12 to 5 daily and his condition improved. The physical examination remained the same.

The patient's condition did not change during 1911. In the early winter he went to Tampa, Florida, and found the climate agreeable, but in February 1912, as the diarrhea had returned, he again went to the hospital for a few days. Except for emaciation and weakness and the presence of numerous furuncles, his condition had changed but little since his previous visit to the hospital. He was much relieved by the rest and soon returned home. In April 1912 he was considerably weakened by a carbuncle. Attention is called to the remarkable duration of this case, as well as of Case H, and to the hereditary history of diabetes of each.

[1]Benedict and Joslin, *loc. cit.*, p. 126.

The urinary record is given in table 9. The records for October 1911 show probably a far nearer approach to the patient's average urinary excretion than the quantities recorded in the hospital. During his stay in the hospital the amount of urine excreted was low, owing to the diarrhea, and possibly because of restrictions in diet, while in October 1911 he was absolutely his own master. The low acidosis is notable and can in a measure be explained by the liberal allowance of carbohydrates in the diet. The reaction of the urine was acid throughout the whole period of observation, and there was but a slight trace of albumen.

EXPERIMENTS WITH CASE I.

Two experiments were reported with this subject in the previous publication; one additional experiment is reported here, for which the bed calorimeter was used. The vital statistics for this subject are as follows:

Date of birth, February 2, 1886; height, 176 cm.; body-weight without clothing during experiment, 49.0 kilos.

TABLE 10.—*Measurements of metabolism—Calorimeter experiment No. I 1.*

Date and period.	Carbon dioxide eliminated.		Oxygen absorbed.		Respiratory quotient.	Average pulse-rate.	Average respiration rate.
	Total.	Per minute.	Total.	Per minute.			
Feb. 23, 1911:	*gms.*	*c.c.*	*gms.*	*c.c.*			
[1]9h 32m a.m. to 10h 17m a.m.	15.7	177	15.6	242	0.73	120	19
10 17 a.m. 11 02 a.m.	14.8	168	15.4	240	.70	120	19
Total 1 hr. 30 mins.[2]	30.5	173	31.0	241	.72	120	19

[1] Subject drank a cup of clear coffee without sugar at 7h 50m a. m.
[2] Carbon dioxide eliminated per kilogram per minute, 4.33 c.c.; oxygen absorbed per kilogram per minute, 6.03 c.c.

CALORIMETER EXPERIMENT NO. I 1.

Date, February 23, 1911. Body-weight without clothing, 40.0 kilos.

Previous to this experiment the subject had taken no food since the evening meal of the day before, with the exception of a cupful of clear coffee, without sugar, at 7h 50m a. m. He arrived at the laboratory at 8h 05m a. m., and entered the bed calorimeter in readiness for the experiment at 8h 53m a. m. The experiment began at 9h 32m a. m., continuing for two 45-minute periods,

TABLE 11.—*Statistics of urine—Calorimeter experiment No. I 1.*

Date and period.	Volume.	Specific gravity.	Total nitrogen.	Sugar.
Feb. 23, 1911:	*c.c.*		*gms.*	*gms.*
[1]7h 00m a.m. to 8h 15m a.m.	133	1.036	0.82	7.8
8 15 a.m. 11 15 a.m.	112	1.037	.80	6.6

[1]Subject drank a cup of clear coffee at 7h 50m a. m., without sugar.

ending at 11h 02m a. m. The subject telephoned twice during the experiment, once at the beginning of the first period and again in the second period, at 10h 40m a. m., when he asked how much longer he would have to stay in the calorimeter. Aside from this he lay very quietly. As the chair calorimeter had been used in the previous experiments with this subject, this was his first experience with the bed calorimeter. He said that he did not find the experiment especially irksome, except that lying still in one position so long made his

back tired. The subject urinated at 7 a. m. before coming to the laboratory, and again at $8^h\ 15^m$ a. m. He defecated at $8^h\ 45^m$ a. m., the feces being copious, watery, and light-colored. Immediately after the experiment was over he defecated again at $11^h\ 15^m$ a. m. No water was taken during the experiment The measurements of the metabolism and urine are given in tables 10 and 11.

CASE J.

DESCRIPTION OF THE CASE.

Male; born March 26, 1889; single; no occupation; onset of diabetes, February 1908; sugar in urine 10 days later; came under our observation September 24, 1909; died, September 17, 1912. The earlier history of this case has already been published.[1]

Later history of the case.—No experiments have been made with this subject other than those previously published. From February 23, 1910, until August 25, 1910, inclusive, the patient remained comfortable. Upon two occasions the effect of oatmeal was tried. In the first trial, July 20–23, 1910, inclusive, the initial day was a vegetable day; upon the two subsequent days 180 grams of carbohydrates were given each day in the form of oatmeal. A positive carbohydrate balance of 55 and 40 grams respectively was obtained in contrast with a positive carbohydrate balance of 5 grams upon the vegetable

TABLE 12.—*Clinical chart—Case J.*

Date.	Volume of urine.	Specific gravity.	Diacetic acid.	Nitrogen.	Ammonia. Total.	Ammonia. $\frac{NH_3-N}{Total\ N}$	Sugar. By copper reduction.	Sugar. By rotation	Diet. Carbohydrate.	Diet. Protein.	Diet. Nitrogen.	Diet. Fat.	Diet. Alcohol.	Diet. Calories.	Carbohydrate balance.	Body weight without clothes.
1910.	*c. c.*			*gms*	*gms.*	*p. ct.*	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*		*gms.*	*kilos.*
Mar. 17–18	2820	1025	+	19 1	..	...	42	56	16	..	...	.....			−25	.
27–28	3240	..	.	10.1		.	33		...	..		....	.	.	.	
28–29	3240	1016	++	..	3 6		+	19	18		..	....	.	.	....	.
Apr. 15–16	2160	1022	0				+	43	21			..				54 5
May 29–30	1800	1031	Sl.+	..			+	40	30	..		...		.	.	54 5
July 1–2	1800	1033	+	...	...	..		50	20	...		....			..	54 0
20–21[1, 2]	2370	1020	++	...	3.5	..	+	14	18	12	2	....	12		+ 5	54.0
21–22[1, 3]	2640	1023	0	5.3	..	.	125	106	180	43	5	144	12	2272	+55	54 5
22–23[1, 3]	2910	1034	Sl.+	7 3	...	..	142	122	180	43	5	144	12	2272	+40	54.5
Aug. 22–23[1, 4]	1980	1023	++	9 6	3.2	27.4	32	20	35	12	2	160±	12	1712	+ 5	
23–24[1, 5]	2490	1027	++	6 2	1 7	22 6	111	95	180	43	7	170±	12	2506	+70	54 0
24–25[1, 6]	1590	1027	+++	8 8	1.1	10.3	28	16	40	90	15	170±	6	2092	+10	54 5

[1] 8 grams of sodium bicarbonate given. [2] Vegetable day.
[3] Oatmeal day, 270 gms. oatmeal, 180 gms. butter, beef tea, 120 gms. wine.
[4] 750 gms. 5 per cent.+6 per cent vegetables, 375 c.c. cream, 105 gms. butter, oil, beef extract, 120 gms. wine.
[5] 270 gms. oatmeal, 180 gms. butter, 125 c.c. cream, beef extract, 120 gms. wine. Feeling quite well.
[6] 2 eggs, bacon, 630 gms. vegetables 5, 6, 10 per cent, 60 gms. pineapple, 300 gms. meat, 30 gms. oil, 375 c.c. cream, 90 gms. butter, 60 gms. wine.

day. The second experiment was made August 22–25, 1910, inclusive. The first day was a vegetable day with 375 c.c. of cream; the second day an oatmeal day in which 180 grams of carbohydrate were taken in the form of oatmeal; on the third day approximately 40 grams of carbohydrate, 90 grams of protein, 6 grams of alcohol, and 170 grams of fat were eaten. The oatmeal produced a positive carbohydrate balance of 70 grams. Upon the vegetable day preceding the oatmeal day the carbohydrate balance was 10 grams. The urinary record for this case is given in table 12. The reaction for the urine was acid throughout. On April 16 and in the July observations the slightest possible trace of albumen was found. In the August observations, however, this had disappeared.

[1] Benedict and Joslin, *loc. cit.*, p. 131.

CASE K.

DESCRIPTION OF THE CASE.

Male; born June 1863; widower; undertaker; onset of diabetes, November 1907; came under our observation August 19, 1908; died in coma November 4, 1910. The early history of the case has previously been published.[1]

On February 24, 1910, the patient reported himself as feeling very well. The quantity of urine was said to be 2000 c.c.

On March 26, 1910, he said that his face felt alternately flushed or numb, and he suffered from both polyphagia and polydipsia. Although on the day previous he had had diarrhea, he was constipated on this day. He was just recovering from an attack of the grippe, from which he had been suffering six weeks. A physical examination on this date gave the following results: Lungs normal; heart, both first and second sounds at the left border of the sternum prolonged; blood-pressure, 115; pulse-rate, 84.

In July 1910, he again entered the hospital. There appeared to be no particular change in his condition, except a loss in weight. His diet had been lax, and he said that he felt better than when on a strict diet. On November 4, 1910, the patient died, having been in coma for about 28 hours. Except for complaints of headache during the previous week, no especial change had been noted in his condition.

The data regarding the urine from March 22 to August 24, 1910, inclusive, are given in table 13. At the times of these observations the urine gave an acid reaction. Very slight traces of albumen were found from July 24 to 28, but none later.

TABLE 13.—*Clinical chart—Case K.*

Date.	Volume.	Specific gravity.	Diacetic acid.	β-oxybutyric acid.	Nitrogen.	Ammonia. Total.	Ammonia. $\frac{NH_3-N}{Total\ N}$	Sugar. By copper reduction.	Sugar. By rotation.	Carbohydrates in diet.	Alcohol in diet.	Carbohydrate balance.	$NaHCO_3$	Body-weight without clothes.
1910.	*c.c.*			*gms.*	*gms.*	*gms.*	*p. ct.*	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*kilos.*
Mar 22–23 ...	2750	1033	Sl.+	....	....	...	. .	...	138	..	..	.....		....
Mar 25–26	2750	1031	Sl.+	..	..	..	.		116		..	.....	.	....
July 24–25..	4500	1029	0	....	25 3	...	.	213	180	..		.....	0	....
July 25–26[1]. ..	2920	1031	+	..	12 0	...		186	[2]175	.	.	.....	0	....
July 26–27.......	2550	1031	++	. ..	14 8	4.9	27 2	142	122	60	12	− 80	0	....
July 27–28.....	**2440**	**1031**	++	..	**16 0**	**5.8**	**29 8**	128	98	**50**	**12**	− 80	**12**	....
July 28–29.....	3030	1030	++++	. ..	15 6	...	. .	175	152	50	12	−125	12	....
July 29–30......	**4560**	.	....	...	**20 1**	.	.	**197**	.	**55**	**18**	**−140**	**20**	....
July 30–31........	4560	....	....	. ..	24.0	...	.	188	...	50	18	−140	20	56.1
July 31–Aug. 1....	3600	1026	+++	.	17 6	...	...	122	115	40	18	− 80	20	55.6
Aug. 1–2	5580	1030	++		17 7	...	.	268	...	55	18	−215	20	....
Aug. 2–3	**4400**	**1028**	....	**30 3**	**17.6**	**3.4**	**15 9**	188	**185**	**50**	**18**	**−140**	20	**55.6**
Aug. 23–24	5000	1030	+	22 0	23.1	...	....	245	240	..	..	.....	..	....

[1]For 19 hrs., from 12 noon July 25 to 7 a.m. July 26. [2]By fermentation method, 178 gms.

EXPERIMENTS WITH CASE K.

One calorimeter experiment and one respiration experiment with this subject were reported in the previous publication. These were both fasting experiments, the chair calorimeter being used in the calorimeter experiment. In this publication three respiration experiments are reported. The vital statistics are as follows:

Date of birth, June 1863; height, 180 cm.; body-weight without clothing during experiments, 55.6 kilos.

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[1]Benedict and Joslin, *loc. cit.*, p. 139.

RESPIRATION EXPERIMENT No. K 1.

Date July 27, 1910. Body-weight without clothing, 55.6 kilos.

The subject came to the laboratory fasting, having had no food since the evening meal of the day before. The experiment included but one period of approximately 15 minutes, beginning at 7h 24m a. m. This period was without incident, the subject remaining very quiet. The results of the experiment may be found in table 14.

RESPIRATION EXPERIMENT No. K 2.

Date, July 29, 1910. Body-weight without clothing, 55.6 kilos.

On the morning of the experiment, the subject came to the laboratory without breakfast and lay down upon the couch at 8h 20m a. m., and the experiment began at 8h 34m a. m., continuing for three periods of 11 to 14 minutes, with intermissions of 8 to 10 minutes. During the first period the subject cleared his throat once, and there was probably a slight loss of air. In the second period he moved his hands several times and his leg once. In the third period he lay quietly the whole time. The results of the experiment are given in table 14.

RESPIRATION EXPERIMENT No. K 3.

Date, August 2, 1910. Body-weight without clothing, 55.6 kilos.

The subject came to the laboratory without breakfast at 7h 30m a. m. and lay down on the couch at 7h 35m a. m. The experiment began at 7h 50m a. m., and continued for three periods of 13 to 15 minutes each, with intermissions of 8 to 13 minutes, ending at 8h 54m a. m. After the close of the second period the pneumograph was loosened, as the subject complained it was too tight. Before the beginning of the third period the subject raised both legs up at the knee, and near the end of this period he straightened out one leg. The results of the experiment are given in table 14.

TABLE 14.—*Results of respiration experiments Nos. K 1–K 3.*

Experiment No.	Date and time.	Duration.	Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse rate.	Average respiration rate.
		min. sec.	c.c.	c.c.			
K 1	July 27, 1910: 7h 24m a.m.	15 41	[1] 182	[1] 257	0.71	77	18
K 2	July 29, 1910:						
	8h 34m a.m.	11 4	179	....	...	74	19
	9 55 a.m.	10 58	187	249	.75	75	18
	10 14 a.m.	14 19	183	258	.71	75	18
	Average		[2] 183	[2] 254	.73	75	18
K 3	Aug. 2, 1910:						
	7h 50m a.m.	12 37	189	267	.71	79	19
	8 11 a.m.	14 37	184	259	.71	83	20
	8 39 a.m.	14 43	188	269	.70	81	19
	Average		[3] 187	[3] 265	.71	81	19

[1] Carbon dioxide eliminated per kilogram per minute, 3.27 c.c.; oxygen absorbed per kilogram per minute, 4.62 c.c.
[2] Carbon dioxide eliminated per kilogram per minute, 3.29 c.c.; oxygen absorbed per kilogram per minute, 4.57 c.c.
[3] Carbon dioxide eliminated per kilogram per minute, 3.36 c.c.; oxygen absorbed per kilogram per minute, 4.77 c.c.

CASE L.

DESCRIPTION OF THE CASE.

Male; born October 18, 1886; single; student; onset of diabetes July 1908; diagnosed as diabetes on December 9, 1908; came under our observation December 15, 1908; condition, November 11, 1912, active work. The earlier details of this case have already been published.[1]

[1] Benedict and Joslin, *loc. cit.*, p. 144.

Between February 24, 1910, and September 28, 1910, the patient remained in excellent condition, and apparently free from sugar most of the time. Although sugar was present in the urine upon April 19, 1911, it disappeared in three days with the limitation of the carbohydrates to 25 grams. A physical examination on this date showed that the blood-pressure (Riva-Rocci) was 100, and that there was a slight systolic murmur at the apex of the heart which was just within the mammillary line. The liver extended one finger's breadth below the costal margin. These findings were confirmed on October 12, 1911. The patient is now (May 1912) doing active work.

The urinary record is given in table 15. The reaction of the urine was acid throughout; there was no albumen present except a very slight trace on April 21–22, 1911. The last sample of urine received from this subject was on May 31, 1912; the reaction was acid, and there was neither albumen nor sugar. On September 21–22, 1910, it will be seen that there were 20 grams of sugar in the urine; on this day he did an unusual amount of physical work.

TABLE 15.—*Clinical chart—Case L.*

Date.	Volume of urine.	Specific gravity.	Diacetic acid.	Nitrogen.	Sugar. By copper reduction.	Sugar. By rotation	Carbohydrates in diet.[1]	Carbohydrate balance.	Body weight without clothing.
1910.	*c.c.*			*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*kilos.*
Sept. 21–22	1875	1028	Sl.+	26.4	20	8	45	+25	67.7
25–26	1750	1022		24.6	6	..	..	..	....
27–28	[2]1500	. .	Sl.+	....	0	..	45	+45	66.5
1911.									
April 18–19	1625	1030	+	..	....	13	45	+30	65.6
21–22	1375	1029	0	26.6	0		25	+25	...
Oct. 11–12	1625	1032	Sl.+	20.2	37.5	26	30	− 5	65.1
1912.									
May 30–31	1750	1022		....		0	..	....	....

[1] No sodium bicarbonate given.

[2] From 7h 30m a.m. to 10h 10m a.m., Sept. 27, 1910, volume of urine, 434 c.c.; specific gravity, 1.016; nitrogen, 2.72 gms.; sugar, 3.7 gms. Another specimen of urine on Sept. 28, 1910, with a specific gravity of 1.022 gave an acid reaction, showed no albumen or sugar, and only a slight trace of diacetic acid.

EXPERIMENTS WITH CASE L.

In the preceding publication five calorimeter experiments with this subject were reported. In four of these the chair calorimeter was used, the other being with the bed calorimeter. Two additional experiments are reported here, both respiration experiments. The vital statistics are as follows:

Date of birth, October 18, 1886; height, 183 cm.; body-weight without clothing during experiments, 66.5 kilos.

RESPIRATION EXPERIMENT No. L1.

Date, September 26, 1910. Body-weight without clothing, 66.5 kilos.

The subject came to the laboratory at 7h 55m a. m. fasting and immediately lay down upon the couch after the pneumograph and stethoscope had been adjusted. As the subject was quite confident that he would be able to stay awake and keep his mouth firmly closed, surgeon's plaster was not used over the mouth in the first period. As the results indicated that there might be a leakage through the mouth, the plaster was used in the last two periods. The experiment began at 9h 12m a. m., and continued for three periods of 13 to 15 minutes, with intermissions of 10 and 12 minutes, ending at 10h 14m a. m. The subject moved his hands and arms occasionally, and changed his position slightly, once putting his hand to his face. Although just previous to the

third period he said that he was not at all tired and was willing to continue indefinitely, there was more movement than in the previous periods. The subject breathed very deeply, which was probably due to the fact that he had been active in athletics while in college and had also sung a great deal. He was considered an extremely good subject, as he was quiet and cooperated intelligently. The results of the experiment are given in table 16.

TABLE 16.—*Results of respiration experiment No. L 1.*

Date and time.	Duration.	Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration rate.
Sept. 26, 1910:	*min. sec.*	*c.c.*	*c.c.*			
9h 12m a.m.	15 17	205	281	0.73	69	8
9 39 a.m.	12 50	207	278	.74	70	9
10 01 a.m.	12 48	204	285	.72	66	7
Average	....	[1] 205	[1] 281	.73	68	8

[1] Carbon dioxide eliminated per kilogram per minute, 3.08 c.c.; oxygen absorbed per kilogram per minute, 4.23 c.c.

RESPIRATION EXPERIMENT NO. L2.

Date, September 27, 1910; body-weight without clothing, 66.5 kilos.

After a breakfast at 7h 45m a. m., consisting of 36 gms. oatmeal (weighed dry), 1.5 ounces of butter, 2 boiled eggs, a cupful of coffee, and half of a grapefruit, the subject came to the laboratory at 8h 35m a. m. He lay down upon the couch at 8h 38m a. m., and the experiment began at 8h 48m a. m. The three 15-minute periods, with intermissions of 14 to 18 minutes, ended at 10h 05m a.m. Surgeon's plaster was used to secure perfect closure of the mouth. After the experiment the subject urinated at 10h 10m a.m. The results of the experiment may be found in table 17.

TABLE 17.—*Results of respiration experiment No. L 2.*

Date and time.	Duration.	Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse rate.	Average respiration rate.
Sept. 27, 1910:	*min. sec.*	*c.c.*	*c.c.*			
[1] 8h 48m a.m.	15 6	241	329	0.73	75	7
9 21 a.m.	15 11	247	337	.73	70	7
9 50 a.m.	15 12	268	336	.80	65	7
Average	....	[2] 252	[2] 334	.75	70	7

[1] Subject ate breakfast at 7h 45m a.m.
[2] Carbon dioxide eliminated per kilogram per minute, 3.79 c.c.; oxygen absorbed per kilogram per minute, 5.02 c.c. The urine collected between 7h 30m a. m. and 10h 10m a.m. amounted to 434 c.c., specific gravity 1.016, and contained 2.72 grams of nitrogen and 3.7 grams of sugar.

CASE M.

DESCRIPTION OF THE CASE.

Male; born January 23, 1853; married; dentist; sugar found in urine in 1900; came under our observation January 6, 1908; condition November 11, 1912, active work. The earlier details of this case have been published in a previous publication.[1]

Later history of the case.—During the winter of 1909 and 1910 the patient insists that he did more work than he ever did in his life before, working even Sundays and until 11 o'clock at night. He used oil freely, often putting it on

[1] Benedict and Joslin, *loc. cit.*, p. 152.

strawberries, oranges, and grapefruit, and even used it on bananas, apples, and cantaloupe. A physical examination July 5, 1910, showed the blood-pressure to be 120; pulse-rate, 96; heart 5 cm. to the right of the median line, the left border lying within the mammillary line, with systolic murmur at the left border of the sternum and at the base. The liver was 2 to 3 fingers' breadth below the costal margin. The spleen was not palpated. On November 28, 1910, the weight was 82.6 kilos., the pulse-rate 84, and the condition good, except for pain in the vicinity of the sixth rib near the mammillary line. This pain resulted from a fall and a possible fracture of the rib. On December 16, 1910, he was considerably shaken up in a railroad accident, besides being exposed to a nervous strain in escaping from an overturned car. It will be seen from table 18, which gives the urinary record, that the quantity of sugar in the urine increased at this time. In May 1911 he took a 5 weeks' vacation trip to Europe. A physical examination gave the same results as previously. On October 3, 1911, the patient had symptoms suggesting an attack of biliary colic. These subsided gradually, however, and after a week's rest recovery was complete. On December 28, 1911, his condition was excellent. An examination showed that no murmur could be heard in the heart. The blood-pressure was 125 and the pulse-rate 88. There was a slight resistance, but no tenderness in the region of the gall-bladder. In the observations made of the urine an acid reaction was shown throughout; there was a slight trace of albumen on January 1, 1911, and a very slight trace on May 15, October 2, and December 23.

TABLE 18.—*Clinical chart—Case M.*

Date.	Volume of urine.	Specific gravity.	Diacetic acid.	Nitrogen.	Sugar.		Body-weight without clothing.
					By copper reduction.	By rotation.	
1910.	*c.c.*			*gms.*	*gms.*	*gms.*	*kilos.*
June 30-July 1......	1340	1028	0	....	..	19	....
July 14-15..........	940	1029	+	16.0	14	6	....
Oct. 1-2...........	890	1027	+	....	..	0	...
1911.							
Dec. 31-Jan. 1[1].....	1450	1030	+	15.5	33	26	..
May 15-16.........	975	1028	Sl. +	13 4	+	8	81.7
Aug 27-28.........	750	1024	0	10.4	0	.	...
Oct. 1-2...........	1200	1024	0	....	+	5	.
Oct. 3-4.	....	1025	0	...	+	[2]0.2	...
Dec. 22-23	950	1027	0	....		3	80 6

[1]β-oxybutyric acid, 1.9 gms.; ammonia, 1.3 gms.; $\frac{NH_3-N}{\text{Total N}}$ =6.9 per cent.; sugar by fermentation, 36 gms.
[2]Per cent.

EXPERIMENTS WITH CASE M.

Three calorimeter experiments with this subject were reported in the previous publication. In two of the experiments the bed calorimeter was used; the chair calorimeter was used in the third. Two additional experiments are reported here, one with the bed calorimeter and one with the respiration apparatus. The vital statistics are as follows:

Date of birth, January 23, 1853; height, 172 cm.; range in body-weight without clothing during experiments, 81.7 to 82.9 kilos.

RESPIRATION EXPERIMENT No. M1.

Date, August 17, 1910. Body-weight without clothing, 81.7 kilos.

This experiment, which was made with the respiration apparatus and with the subject fasting, included four separate periods of 10 to 11 minutes each,

with intermissions ranging from 11 to 19 minutes. The experiment began at $8^h 13^m$ a. m., and ended at $9^h 39^m$ a. m. The subject was instructed not to go to sleep and apparently did not; in the second period he was uneasy, moving his legs and changing his position somewhat several times. In the third period the observer thought the subject opened his mouth and moistened his lips, but he himself thought he did not. The results of the experiment are given in table 19.

TABLE 19.—*Results of respiration experiment No. M 1.*

Date and time.	Duration.	Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration rate.
Aug. 17, 1910:	*min. sec.*	*c.c.*	*c.c.*			
$8^h 13^m$ a.m. . .	10 50	197	. . .	. . . .	76	9
8 43 a.m. . .	11 10	200	271	0.74	76	9
9 08 a.m. . . .	10 9	187	256	.73	74	10
9 29 a.m. . . .	10 25	203	260	.78	[1] 74	9
Average . . .	. . . . .	[2] 197	[2] 262	.75	75	9

[1] One record of pulse.
[2] Carbon dioxide eliminated per kgm. per minute, 2.41 c.c.; oxygen absorbed per kgm. per minute, 3.21 c.c. The 100 c.c. of urine collected between $6^h 45^m$ a.m. and $9^h 45^m$ a.m. contained 1.56 gm. nitrogen and 1 gm. sugar.

CALORIMETER EXPERIMENT M 2.

Date, June 15, 1911. Body-weight without clothing, 82.9 kilos.

The subject came to the laboratory without breakfast at $7^h 25^m$ a. m., entered the bed calorimeter at $7^h 56^m$ a. m., and the experiment began at $8^h 52^m$ a. m. Three periods, one of 53 minutes and two of 45 minutes, were included in this experiment. Except in the second period, when he rolled over on his side and used his arms considerably in handling the newspaper he was reading, the subject was very quiet all through the experiment. Afterwards he said he was very comfortable while in the apparatus and suffered no discomfort. The metabolism measurements are given in table 20.

TABLE 20.—*Measurements of metabolism—Calorimeter experiment No. M 2.*

Date and period.	Carbon dioxide eliminated.		Oxygen absorbed.		Respiratory quotient.	Average pulse-rate.	Average respiration rate.
	Total.	Per minute.	Total.	Per minute.			
June 15, 1911:	*gms.*	*c.c.*	*gms.*	*c.c.*			
$8^h 52^m$ a.m. to $9^h 45^m$ a.m.	19.7	190	18.0	239	0.79	70	11
9 45 a.m. 10 30 a.m.	16.6	189	15.7	244	.77	68	
10 30 a.m. 11 15 a.m.	17.0	192	15.9	248	.78	67	. .
Total 2 hrs. 23 min.[1]	53.3	190	49.6	243	.78	68	. .

[1] Carbon dioxide eliminated per kilogram per minute, 2.29 c.c.; oxygen absorbed per kilogram per minute, 2.93 c.c. The urine collected between about $10^h 30^m$ p.m. June 14 and $12^h 15^m$ p.m. June 15, specific gravity 1.025, amounted to 335 c.c. and contained 4.12 gms. of nitrogen and 3.6 gms. of sugar.

CASE N.

DESCRIPTION OF THE CASE.

Male; born August 1, 1896; developed diabetes just before 13 years of age in July 1909, and came under our observation August 1909; died in coma February 16, 1911.

Family history.—Grandmother died of diabetes at the age of 78. The patient was an only child, and his father and mother are well.

Past history.—Measles.

Present illness.—Early in June 1909 the boy began losing weight while riding a new bicycle. During the first part of August, frequent micturition developed and in the course of a few days he began to droop.

Physical examination.—Height, 146 cm.; greatest weight, 34.5 kilos.; weight August 28, 1909, 29.6 kilos. Fairly well developed. Pupils equal and reacted to light. Tongue and teeth normal. Lungs normal. Heart extended 2 cm. to right of median line and 9 cm. to left of median line (just external to mammillary line). Systolic murmur at apex. The liver extended 2 fingers' breadth below the costal margin. Knee-jerks normal. No edema.

Urine data.—The greatest quantity of urine observed was at the onset, when it reached 3500 c.c. The patient's urine contained 6.6 per cent of sugar on August 28 and, on the following day, 162 grams were excreted. By the restriction of the diet to 20 grams carbohydrate, the urine became sugar-free on September 13 and this condition was maintained almost constantly until November 22, 1909; he then evidently broke diet and the sugar in the urine went up to 7 per cent (88 grams).

The sugar did not again disappear from the urine until December 15, when the patient was at the hospital. It remained absent for the 4 days he was there, returning promptly when he left the institution, and never disappeared save upon two days in January and one in February of the following year.

Albumen was either absent or present only in extremely small quantities; during the last few months of life but a trace was present.

The urine was invariably acid, save upon one day, December 18, 1909. During the first period of observation, from August 1909 until April 1910, the signs of acidosis were slight and represented at the most by only a moderate reaction for diacetic acid. From that time on they increased, and the acidosis was extreme in November 1910, when the patient was again in the hospital. At this time the urinary record (table 21) shows 35 grams of β-oxybutyric acid in one day, and on the same day 4.2 grams of ammonia.

Death finally occurred on February 16, 1911, after 3 days of coma. The case therefore affords a most excellent example for a study of diabetes with and without acidosis. During its duration of 19 months, the disease ran a course free from complication, with the exception of the persistent ulceration of one incisor tooth.

EXPERIMENTS WITH CASE N.

With this subject, eight calorimeter experiments were made, in all of which the bed calorimeter was used. In seven experiments the subject entered the apparatus without breakfast, after a 12 hours' fast. One experiment was made following a breakfast of cooked oatmeal. In addition, one respiration experiment was carried out with this subject. The data for the calorimeter experiments are compared in table 33. The vital statistics were as follows:

Date of birth, August 1, 1896; height, 146 cm.; range in body-weight without clothing during experiments, 30.5 to 32.5 kilos.

RESPIRATION EXPERIMENT No. N 1.

Date, August 18, 1910. Body-weight without clothing, 32.5 kilos.

In this experiment the respiratory exchange was determined by means of the respiration apparatus, the subject lying on a couch. It is probable that he took food previous to the experiment. The experiment began at $8^h 12^m$ a.m., covering one 10-minute period and ending at $8^h 22^m$ a.m. The subject was

TABLE 21.— *Clinical chart—Case N.*

Date.	Volume of urine.	Specific gravity.	Diacetic acid.	β-oxybutyric acid.	Nitrogen.	Ammonia.		Sugar.		Carbohydrate in diet.	Carbohydrate balance.	$NaHCO_3$.	Body-weight without clothing.
						Total.	$\frac{NH_3-N}{Total\ N}$	By copper reduction.	By rotation.				
1909.	c.c.			gms.	gms.	gms.	p. ct.	gms.	gms.	gms.	gms.	gms	kilos.
Aug. 27–28	....	1032	0	....	....	...	....	...	16.6	..	.....	..	29.6
Aug. 29–30	2530	1034	0	....	13.5	...	....	...	162	55±	−105	0	29.9
Aug. 30–31	3000	....	0	....	....	...	....	...	156	..	.....	0	29.9
Sept. 1– 2	2625	1029	0	....	....	...	....	...	110	..	.....	0	30.1
Sept. 2– 3	2250	1030	Sl.+	....	....	...	....	...	95	..	.....	..	....
Sept. 3– 4	2750	1031	0	....	....	...	....	...	138	..	.....	..	30.2
Sept. 7– 8	2125	1028	0	....	....	...	....	...	85	..	.....	0	....
Sept. 8– 9	1750	1025	Sl.+	....	....	...	....	...	28	..	.....	0	30.1
Sept. 9–10	1500	1021	Sl.+	....	....	...	....	...	6	..	.....	0	30.2
Sept. 10–11	1625	1017	Sl.+	....	....	...	....	...	3	..	.....	0	30 4
Sept. 12–13	750	1021	Sl.+	....	....	...	....	...	0	20	.....	0	30.4
Sept. 16–17	1000+	1019	0	....	....	...	....	0	...	20	+ 20	0	30 5
Sept. 22–23	2000	1015	0	....	....	...	....	...	6		.....	0	31.6
Sept. 24–25	2250	1017	0	....	....	...	....	...	9		.....	0	31.2
Sept. 26–27	1500	1015	0	....	....	...	....	0	...	..	.....	0	....
Oct. 10–11	1250	....	0	....	....	...	....	0	...	20	+ 20	0	33.4
Oct. 17–18	....	....	0	....	....	...	....	0	...		.....	0	33 0
Oct. 24–25	1000+	1019	0	....	....	...	....	...	12	..	.....	0	32.8
Oct. 31–Nov. 1	1250	....	0	....	....	...	....	0	...	..	.....	0	33.1
Nov. 9–10	750	1018	0	....	....	...	....	0	...	30	+ 30	0	33.0
Nov. 21–22	1250+	1037	0	....	....	...	....	+	88	..	.....	0	33.4
Nov. 23–24	750	1029	0	....	....	...	....	+	18	..	.....	0	....
Nov. 25–29	1500+	1027	0	....	....	...	....	+	54	..	.....	0	....
Dec. 1– 2	1000	1024	0	....	....	...	....	+	8	..	.....	0	33.2
Dec. 8– 9	1000	1026	0	....	....	...	....	+	20	..	.....	0	....
Dec. 12–13	1250	1035	0	....	....	...	....	+	53	..	.....	0	33.4
Dec. 15–16	900	1023	0	....	....	...	....	0	0	20	+ 20	0	32.1
Dec. 19–20	1750	1020	0	....	....	...	....	+	14		.....	0	33.7
1910.													
Jan. 2– 3	1250	1020	0	....	....	...	....	+	5	..	.....	..	....
Jan. 6– 7	1500	1025	Sl.+	....	....	...	....	...	18	..	.....	0	33.7
Jan. 9–10	750	1026	Sl.+	....	....	...	....	+	5	..	.....		....
Jan. 17–18	....	1014	0	....	....	...	....	0	...	..	.....	..	....
Feb. 3– 4	1000	1021	....	....	....	...	....	+	10	..	.....	0	....
Feb. 10–11	750	1024	0	....	....	...	....	0	...	..	.....	0	34.0
Mar. 4– 5	875	1022	+	....	....	...	....	..	4	..	.....	0	33.3
Mar. 29–30	1250	1036	Sl.+	....	....	...	....	+	85	..	.....	0	....
Apr. 10–11	1625	1035	Sl.+	....	....	...	....	...	111	..	.....	0	33.8
Apr. 17–18	1375	1027	++	....	....	...	....	+	30		.....	0	33.0
May 1– 2	1700	1033	+	....	....	...	....	+	95		.....	0	33.2
May 15–16	2000	1034	0	...	...	...	....	+	104	..	.....	0	....
May 23–24	1375	1034	+	....	7 9	1.7	17.7	..	66	..	.....	4	32 7
June 6– 7	2170	1025	Sl.+	...	9 4	...	....	65	61	..	.....	4	32.3
July 1– 2	1530	1034	++	....	....	...	....	+	89	..	.....	4	32.0
July 14–15	1375	1032	++	....	....	2.0	....	[2]51	50	..	.....	4	....
July 31–Aug. 1	1560	1030	+++	....	....	...	....	...	103	..	.....	4	....
Aug. 8– 9	1750	1031	++++	....	12 1	2.5	17.0	72	60	..	.....	4	30.8
Aug. 23–24	2125	1035	++	....	13.5	.	....	103	119	..	.....	8	31.3
Aug. 30–31	2160	1030	++	....	11 8	. .	....	84	78	..	.....	..	30.8
Sept. 2– 3	1250	1036	++++	....	....	..	....	...	45		.....	..	....
Sept. 11–15	1875	1033	+++	....	....	.	....	...	83		.....	..	31.9
Nov. 15–16	[3]1750	....	++++	....	....	...	....	+	46		.....	..	....
Nov. 21–22[4]	....	1033	++	....	....	...	....	...	112	..	.....	..	....
Nov. 22–23	2750	1028	++++	....	....	...	....	...	94	80	− 15	20	....
Nov. 23–24	2740	1027	++++	....	....	...	....	...	93	80	− 15	20	32.3
Nov. 24–25	2880	1029	++++	....	....	...	....	...	92	80	− 10	20	32 4
Nov. 25–26	2620	1026	++++	..	....	2.1	....	...	79	80	.....	20	32 3
Nov. 26–27	2900	1024	++++	28.9	....	...	....	...	64	15	− 50	20	32.4
Nov. 27–28	2960	1028	++++	....	....	...	....	...	89	55	− 35	20	32.7
Nov. 28–29	2780	1024	++++	...	10.4	2.8	22 1	..	67	55	− 10	20	32.0
Nov. 29–30	3120	1021	+++	..	....	2 4	..	69	62	55	− 15	20	31.8
Nov. 30–Dec. 1	[5]2940	1021	++++	35 0	8.2	4 2	42 1	41	35	15	− 25	20	....
Dec. 1– 2	[6]3000	1020	+++	...	6.2	3 0	39.8	69	60	135	+ 65	16	30.1
Dec. 2– 3	2212	1023	++++	....	6.2	2 7	35 8	58	49	45	− 15	20	30.8
Dec. 3– 4	1310	1020	+++	....	5.1	1.6	25 8	33	33	30	− 10	..	31 4
Dec. 4– 5	2540	1021	+++++	....	10.7	2 3	17.7	77	68	35	− 40	..	32 3
Dec. 5– 6	2950	1022	++	30.6	9.7	2 3	19.5	41	41	35	− 5	..	32.1
Dec. 6– 7	2840	1023	+++	26 5	10.1	2 3	18.7	61	51	35	− 25	..	32 1
Dec. 7– 8	2005	1025	++++	22 3	7 7	1 8	19.2	53	40	45	− 10	20	32.4
Dec. 8– 9	2600	1027	++++	15 1	6.8	1.6	19.4	117	104	45	− 70	20	32 3
Dec. 9–10	2500	1029	+++	20.7	5.3	1 6	24.8	138	125	45	− 95	16	31.8
Dec. 10–11	3135	1030	++	21.8	8.0	2 8	28.8	180	163	45	−135	15	31.4
Dec. 11–12	2760	1032	+	16 9	8.1	2.3	23.4	163	155	45	−120	16	31.8
Dec. 12–13	2510	1026	+++	21.2	8 0	2 4	24 7	98	95	145	+ 45	16	31.5
Dec. 13–14	2650	1022	+++	18.3	10.1	2 3	18.7	56	53	45	− 10	16	31.4
Dec. 14–15	2450	...	....	....	9.5	...	....	70	.	45	− 25	16	....
Dec. 16–17	3000	1024	+++	....	....	2.2	....	+	78	45	− 35	..	30.3
Dec. 23–24	2170	1031	++	....	....	...	....	+	78	55	− 25	..	30.2
Dec. 27–28	1875	1029	++++	....	....	1 2	....	+	45	..	.....	..	....
1911.													
Jan. 6– 7	[3]2375	1032	+++	....	....	...	....	+	105	..	.....	..	....
Jan. 19–20	2250	1026	+++	....	....	...	....	...	63	..	.....	..	30.6
Feb. 5– 6	2375	1026	++++	....	....	...	....	...	62	..	.....	..	....
Feb. 15–16	[7]330	1019	0	....	....	...	....	+	4		.....		....

[1] Per cent. [2] By fermentation. [3] Many fine and coarse granular casts in urinary sediment.
[4] Less than 24 hrs. [5] Period of 23 hrs. 45 min. Vegetable day, including 240 c.c. cream.
[6] Period of 24 hrs. 15 min., 192 gms. oatmeal, 240 c.c. cream.
[7] 3 hrs. Many casts, chiefly coarse granular, in urinary sediment.

reported as being restless, opening his mouth once and raising his hand to his face. Before coming to the laboratory the subject urinated at 5 a. m., and after the experiment was over he urinated at $8^h\ 50^m$ a. m. The carbon dioxide eliminated per minute was 181 c.c., and per kilogram per minute 5.57 c.c. The oxygen absorbed per minute was 237 c.c. per minute, and per kilogram per minute, 7.29 c.c. The respiratory quotient was 0.76. During the experimental period the pulse-rate averaged 73 and the respiration-rate, 17. The urine collected between 5 a. m. and $8^h\ 50^m$ a. m. amounted to 145 c.c. and contained 0.67 gram of nitrogen and 7.1 grams of sugar.

Calorimeter Experiment No. N 2.

Date, December 1, 1910. Body-weight without clothing, 31.2 kilos.

For this experiment, the subject came to the laboratory without breakfast at $7^h\ 05^m$ a. m., and entered the bed calorimeter at $7^h\ 17^m$ a. m. The experiment began at $8^h\ 04^m$ a. m., and continued for three 45-minute periods, ending at $10^h\ 19^m$ a. m. The pulse and respiration rates were obtained by the usual methods, but no records of the body-temperature were made. The subject was very quiet, lying on his back and reading throughout the whole experiment. Two samples of the alveolar air were taken both before and after the experiment. Before coming to the laboratory, the subject urinated at $6^h\ 45^m$ a. m., and again after the experiment at $10^h\ 28^m$ a. m. The records of the experiment are given in tables 22 and 25.

TABLE 22.—*Measurements of metabolism—Calorimeter experiment No. N 2.*

Date and period.	Carbon dioxide eliminated.		Oxygen absorbed.		Respiratory quotient.	Average pulse-rate.	Average respiration rate.
	Total.	Per minute.	Total.	Per minute.			
Dec. 1, 1910:	*gms.*	*c.c.*	*gms.*	*c.c.*			
$8^h\ 4^m$ a.m. to $8^h\ 49^m$ a.m.	12.6	143	10.8	168	0 85	76	17
8 49 a.m. 9 34 a.m	11 8	133	12.8	199	.67	78	18
9 34 a.m. 10 19 a.m.	11.0	126	11.0	171	.73	[1] 72	19
Total 2 hrs. 15 min.[2]	35 4	133	34.6	179	....	.	

[1] One record at $10^h\ 03^m$ a.m.

[2] Carbon dioxide eliminated per kilogram per minute, 4.26 c.c.; oxygen absorbed per kilogram per minute, 5.74 c.c.

Calorimeter Experiment No. N 3.

Date, December 2, 1910. Body-weight without clothing, 30.9 kilos.

On the morning of the experiment the subject ate a breakfast consisting of 300 grams of cooked oatmeal and came to the laboratory at $7^h\ 55^m$ a. m. At $8^h\ 10^m$ a. m. he entered the respiration chamber of the bed calorimeter; the experiment began at $8^h\ 48^m$ a. m. and continued for two 45-minute periods and one 53-minute period, ending at $11^h\ 11^m$ a. m. In the first period he lay very quietly on his back, reading, but did not read in the second period and moved slightly two or three times; he seemed to be asleep near the end of the period. At the beginning of the third period he was asleep, but soon awoke and read for a short time, then lay quietly without reading. According to the observer's record, the subject moved considerably more in this period than in the two preceding, and it was necessary to extend the period 8 minutes in order to obtain satisfactory temperature equilibrium at the end. Samples of alveolar air were taken before and after the experiment. The subject urinated at 7 a. m. before coming to the laboratory and again at $11^h\ 26^m$ a. m. after the experiment was over. The records for the experiment are given in tables 23 and 25.

TABLE 23.—*Measurements of metabolism—Calorimeter experiment No. N 3.*

Date and period.	Carbon dioxide eliminated.		Oxygen absorbed.		Respiratory quotient.	Average pulse rate.	Average respiration rate.
	Total.	Per minute.	Total.	Per minute.			
Dec. 2, 1910:	*gms.*	*c.c.*	*gms.*	*c.c.*			
[1]8h 48m a.m. to 9h 33m a.m...	12.4	140	11.7	182	0.77	79	17
9 33 a.m. 10 18 a.m..	11.9	134	11.4	178	.76	81	14
10 18 a.m. 11 11 a.m....	14.4	139	13.8	182	.76	84	16
Total 2 hrs. 23 min.[2].......	38.7	138	36.9	181	.		...

[1] Subject ate 300 gms. of cooked oatmeal about 1 hr. 30 min. before the experiment began.
[2] Carbon dioxide eliminated per kilogram per minute, 4.47 c.c.; oxygen absorbed per kilogram per minute, 5.86 c.c.

CALORIMETER EXPERIMENT No. N 4.

Date, December 3, 1910. Body-weight without clothing, 30.5 kilos.

When the subject came to the laboratory at $7^h 02^m$ a. m. on the experimental day, aside from a small cupful of black coffee he had had no food since the evening meal of the day before. After two samples of alveolar air had been taken, he entered the bed calorimeter at $7^h 23^m$ a. m. The experiment began at $8^h 08^m$ a. m., continued for three 45-minute periods, and ended at $10^h 23^m$ a. m. The subject was very quiet throughout the experiment, reading most of the time except near the end of each period; he did not sleep at all. After the experiment was over, he urinated at $10^h 35^m$ a. m.; two additional samples of alveolar air were also taken. The subject said that he did not feel quite so tired and hungry as he had at the close of preceding experiments. On the morning of December 5 his mother said that during the afternoon of the experimental day and all the next day the subject was much brighter and better than he had been for some time. He was quite lively and in good spirits,

TABLE 24.—*Measurement of metabolism—Calorimeter experiment No. N 4.*

Date and period.	Carbon dioxide eliminated.		Oxygen absorbed.		Respiratory quotient.	Average pulse-rate.	Average respiration rate.
	Total.	Per minute.	Total.	Per minute.			
Dec. 3, 1910:	*gms.*	*c.c.*	*gms.*	*c.c.*			
[1]8h 08m a.m. to 8h 53m a.m..	11.0	124	10.8	168	0.74	56	14
8 53 a.m. 9 38 a.m......	10.2	116	9.8	152	.76	58	14
9 38 a.m. 10 23 a.m.....	11.0	124	10.3	161	.77	55	13
Total 2 hrs. 15 mins.[2]........	32.2	121	30.9	160	....		..

[1] Subject drank a small cup of black coffee about 1 hr. 15 mins. before the experiment began.
[2] Carbon dioxide eliminated per kilogram per minute, 3.97 c.c.; oxygen absorbed per kilogram per minute, 5.25 c.c.

TABLE 25.—*Statistics of urine—Calorimeter experiments Nos. N 2–N 4.*

Date and period.	Volume.	Specific gravity.	Total nitrogen.	Sugar.
	c.c.		*gms.*	*gms.*
Dec. 1, 1910: 6h 45m a.m. to 10h 38m a.m......	473	1.019	1.26	5.7
Dec. 1–2, 1910: 10h 38m a.m. to 7h a.m......	2520	1.020	4.86	64.8
Dec. 2, 1910: 7 a.m.[1] to 11h 26m a.m...........	512	1.022	.98	17.9
Dec. 2–3, 1910: 11h 26m a.m. to 7 a.m.......	1700	...	5.09	40.6
Dec. 3, 1910: 7 a.m.[2] to 10h 35m a.m.........	250	1.030	.95	8.1
Dec. 3–4, 1910: 10h 35m a.m. to 7 a.m..........	1560	....	4.11	29.4

[1] Subject ate 300 gms. of cooked oatmeal just before coming to the laboratory at $7^h 55^m$ a. m.
[2] Subject drank a small cup of black coffee just before coming to the laboratory at $7^h 02^m$ a.m.

although previously he had been very melancholy and his physical condition had preyed upon his mind so that he had not been at all happy. The measurements of metabolism and the average pulse and respiration rates are given in table 24, and the statistics of urine in table 25.

Calorimeter Experiment No. N 5.

Date, December 5, 1910. Body-weight without clothing, 31.7 kilos.

For this experiment the subject came to the laboratory at 7h 05m a. m., without breakfast, and entered the bed calorimeter at 7h 29m a. m.; the experiment began at 8h 22m a. m., ending at 10h 38m a. m., after three 45-minute periods. Throughout the whole period the subject was quiet, reading much of the time. Samples of the alveolar air were taken both before and after the experiment. The subject urinated at 7 a.m., before coming to the laboratory, and at 10h 56m a. m. after the experiment was over. He said at the conclusion of the experiment that, while he was tired and sleepy and somewhat hungry, he felt quite well. The records of the experiment are given in table 26.

Table 26.—*Measurements of metabolism—Calorimeter experiment No. N 5.*

Date and period.	Carbon dioxide eliminated.		Oxygen absorbed.		Respiratory quotient.	Average pulse-rate.	Average respiration rate.
	Total.	Per minute.	Total.	Per minute.			
Dec. 5, 1910—	*gms.*	*c.c.*	*gms.*	*c.c.*			
8h 22m a.m. to 9h 07m a.m.	11.2	127	11.1	172	0.74	54	16
9 07 a.m. 9 52 a.m.	10.5	119	11.1	172	.69	55	16
9 52 a.m. 10 38 a.m.	11.9	132	11.1	168	.78	58	16
Total 2 hrs. 16 min.[1]	33.6	126	33.3	171	...		..

[1] Carbon dioxide eliminated per kilogram per minute, 3.97 c.c.; oxygen absorbed per kilogram per minute, 5.39 c.c. The urine collected between 7 a.m. and 10h 56m a.m. amounted to 590 c.c. and contained 1.96 gms. of nitrogen and 8.8 gms. of sugar.

Calorimeter Experiment No. N 6.

Date, December 7, 1910. Body-weight without clothing, 32 kilos.

The subject arrived at the laboratory without breakfast at 7h 05m a. m. The experiment began at 8h 20m a. m. and continued for three 45-minute periods, ending at 10h 35m a. m. Throughout the experiment the subject lay on his back, quietly reading. He did not sleep at all. As usual samples of alveolar air were taken before and after the experiment. Before coming to the laboratory the subject urinated at 6h 30m a. m. and at 10h 50m a. m., after the experiment was over. On coming out of the bed calorimeter the subject complained of no discomfort, saying only that he was quite hungry. The records of the experiment are given in table 27.

Table 27.—*Measurements of metabolism—Calorimeter experiment No. N 6.*

Date and period.	Carbon dioxide eliminated.		Oxygen absorbed.		Respiratory quotient.	Average pulse-rate.	Average respiration rate.
	Total.	Per minute.	Total.	Per minute.			
Dec. 7, 1910:	*gms.*	*c.c.*	*gms.*	*c.c.*			
8h 20m a.m. to 9h 05m a.m.	11.4	129	11.2	174	0.74	56	17
9 05 a.m. 9 50 a.m.	12.2	139	11.7	181	.77	57	17
9 50 a.m. 10 35 a.m.	10.9	122	11.1	172	.71	57	16
Total 2 hrs. 15 min.[1]	34.5	130	34.0	176	..	..	.

[1] Carbon dioxide eliminated per kilogram per minute, 4.06 c.c.; oxygen absorbed per kilogram per minute, 5.50 c.c. The urine collected between 6h 30m a.m. and 10h 50m a.m. amounted to 545 c.c., specific gravity 1.019, and contained 1.90 gms. of nitrogen and 7.9 gms. of sugar.

CALORIMETER EXPERIMENT No. N 7.

Date, December 10, 1910. Body-weight without clothing, 31.8 kilos.

The subject arrived at the laboratory at $7^h\ 10^m$ a. m., without breakfast. Before he entered the bed calorimeter at $7^h\ 33^m$ a. m., samples of alveolar air were taken and a record made of the ventilation of the lungs. The experiment began at $8^h\ 22^m$ a. m., ending at $10^h\ 40^m$ a. m., after three 45-minute periods. At $9^h\ 56^m$ a. m. the subject drank 76 c.c. of water. During the first period he

TABLE 28.—*Measurements of metabolism—Calorimeter experiment No. N 7.*

Date and period.	Carbon dioxide eliminated.		Oxygen absorbed.		Respiratory quotient.	Average pulse-rate.	Average respiration rate.
	Total.	Per minute.	Total.	Per minute.			
Dec. 10, 1910:	*gms.*	*c.c.*	*gms.*	*c.c.*			
$8^h\ 22^m$ a.m. to $9^h\ 07^m$ a.m ...	12 9	146	11 9	184	0.79	75	19
9 07 a.m. 9 54 a.m.. .	12 6	137	12 4	184	75	77	18
9 54 a.m. 10 40 a.m.. .	13.0	143	12 6	192	75	81	18
Total 2 hrs. 18 min.[1]	38 5	142	36.9	187	....	..	..

[1] Carbon dioxide eliminated per kilogram per minute, 4.47 c.c.; oxygen absorbed per kilogram per minute, 5.88 c.c

was very quiet, reading. He did not read during the second period, but lay very quietly, and slept about 20 minutes. In the third period, however, he moved considerably and gave evidence of being very restless. Samples of the alveolar air were also taken after the experiment. The subject urinated before the experiment at $6^h\ 45^m$ a. m. and after the experiment at $11^h\ 05^m$ a. m. The data regarding the metabolism measurements and the average pulse and respiation rates are given in table 28 and the statistics of urine in table 29.

TABLE 29.—*Statistics of urine—Calorimeter experiment No. N 7.*

Date and period.	Volume.	Specific gravity.	Total nitrogen.	Sugar.
	c.c.		*gms.*	*gms.*
Dec. 10, 1910: $6^h\ 45^m$ a.m. to $11^h\ 05^m$ a.m......	475	1 027	1.47	15 2
Dec. 10–11, 1910: $11^h\ 05^m$ a.m. to $6^h\ 45^m$ a.m...........	2660	1.031	6.66	164.0

CALORIMETER EXPERIMENT No. N 8.

Date, December 12, 1910. Body-weight without clothing, 31.7 kilos.

The subject reached the laboratory at 7 a. m., without breakfast, and entered the bed calorimeter at $7^h\ 38^m$ a. m., after two samples of the alveolar air had been taken and records made of the ventilation of the lungs. A blood-pressure of 90 mm. was also recorded at $7^h\ 30^m$ a. m. The experiment began at 9 a. m., continuing for two 30-minute and one 40-minute periods, ending at $10^h\ 40^m$ a. m. The pulse and respiration rates were obtained as usual by the stethoscope and pneumograph. The telephone was used once during the experiment, at the beginning of the first period, but otherwise the subject was very quiet, reading nearly all of the time except near the end of each period. Samples of the alveolar air were taken at the end of the experiment, as usual. Before coming to the laboratory, the subject urinated at $6^h\ 45^m$ a. m., and again at $11^h\ 08^m$ a. m., after the experiment was over. No water was taken during the experiment. The data regarding the metabolism measurements and the average pulse and respiration rates are given in table 30 and the statistics of urine in table 31.

Calorimeter Experiment No. N 9.

Date, December 14, 1910. Body-weight without clothing, 31.4 kilos.

The subject arrived at the laboratory without breakfast at 7h 10m a. m., and entered the bed calorimeter at 7h 32m a. m. The experiment began at 8h 21m a. m., continuing for two 45-minute periods and one 40-minute period, ending at 10h 31m a. m. As usual with this subject, he lay quietly reading during practically the whole experiment, save at the beginning of the third period, when he moved quite a little. Samples of alveolar air were taken and records made of the ventilation of the lungs both before and after the experiment; a record of 90 mm. for the blood-pressure was obtained at 7h 10m a. m. The subject urinated at 7 a. m., before coming to the laboratory, and at 10h 55m a. m., after the experiment was over. No water was taken. The results of the experiment are given in table 32.

Table 30.—*Measurements of metabolism—Calorimeter experiment No. N 8.*

Date aad period.	Carbon dioxide eliminated.		Oxygen absorbed.		Respiratory quotieat.	Average pulse-rate.	Average respiration rate.
	Total.	Per minute.	Total.	Per minute.			
Dec. 12, 1910:	*gms.*	*c.c.*	*gms.*	*c.c.*			
9h 00m a.m. to 9h 30m a.m.	8.0	135	8.2	192	0.70	59	15
9 30 a.m. 10 00 a.m.	7.5	127	7.5	173	.73	61	15
10 00 a.m. 10 40 a.m.	10.0	128	10.1	176	.72	61	15
Total 1 hr. 40 min.[1]	25.5	130	25.8	181	..	..	..

[1] Carbon dioxide eliminated per kilogram per minute, 4.10 c.c.; oxygen absorbed per kilogram per minute, 5.71 c.c.

Table 31.—*Statistics of urine—Calorimeter experiment No. N 8.*

Date and period.	Volume.	Specific gravity.	Total nitrogen.	Sugar.
Dec. 12, 1910:	*c.c.*		*gms.*	*gms.*
6h 45m a.m. to 11h 08m a.m.	350	1.032	1.84	16.7
Dec. 12–13, 1910:				
11h 08m a.m. to 6h 45m a.m.	2160	1.026	5.90	80.0

Table 32.—*Measurements of metabolism—Calorimeter experiment No. N 9.*

Date aad period.	Carbon dioxide elimiaated.		Oxygen absorbed.		Respiratory quotient.	Average pulse-rate.	Average respiration rate.
	Total.	Per minute.	Total.	Per miaute.			
Dec. 14, 1910:	*gms.*	*c.c.*	*gms.*	*c.c.*			
8h 21m a.m. to 9h 06m a.m.	11.0	126	10.9	169	0.74	61	14
9 06 a.m. 9 51 a.m.	10.8	121	12.0	187	.65	58	15
9 51 a.m. 10 31 a.m.	9.6	121	9.4	164	.74	58	14
Total 2 hrs. 10 mia.[1]	31.4	123	32.3	174	...		..

[1] Carbon dioxide eliminated per kilogram per minute, 3.92 c.c.; oxygen absorbed per kilogram per minute, 5.54 c.c. The urine collected betweea 7 a.m. and 10h 55m a.m. amounted to 390 c.c., specific gravity 1.025, and contained 1.49 gms. of nitrogea aad 10.6 gms. of sugar.

CASE O.

DESCRIPTION OF THE CASE.

Female; born August 16, 1894; single; no occupation; onset of diabetes at age of 13, February 1908; sugar in urine, March 1908; came under our observation April 18, 1908; died in coma December 10, 1910.

Family history.—No history of diabetes in the family. Father died of pneumonia; mother and brother well.

Past history.—Scarlet fever, dysentery at 3 years of age, measles, mumps, whooping-cough, chicken-pox, enuresis nocturna which ceased at the age of 4. Had always a voracious appetite, sometimes eating six potatoes at a meal; ate much candy.

General history of the case.—During the year preceding the onset of the disease the patient developed rapidly both in height and weight. In February 1908, she showed weariness. Early in March, polydipsia, polyuria, and polyphagia were present, and sugar was demonstrated in the urine. One year previous the urine had been examined and was said to be normal.

During the whole period of illness the patient remained in good condition and attended school with comfort. The diet was rigidly adhered to and not relaxed except when the diagnosis was at one time doubted by the local physician. Catamenia was established for the first time in March 1909. No essential change in the physical examination took place. The patient died in coma on December 10, 1910.

TABLE 33.—*Comparison of metabolism experiments in bed calorimeter with Case N.*

EXPERIMENTS WITHOUT FOOD.

Experiment No.	Date.	Weight of subject.	Length of experiment.	Per minute.		Respiratory quotient.	Average pulse per minute.	Average respiration per minute.
				Carbon dioxide eliminated.	Oxygen absorbed.			
	1910.	*kilos.*	*hr. min.*	*c.c.*	*c.c.*			
N 2	Dec. 1	31.2	2 15	133	179	0.74	75	18.0
N 4	Dec. 3[1]	30.5	2 15	121	160	.76	57	13.5
N 5	Dec. 5	31.7	2 16	126	171	.73	56	16.0
N 6	Dec. 7	32.0	2 15	130	176	.74	57	16.5
N 7	Dec. 10	31.8	2 18	142	187	.76	78	18.5
N 8	Dec. 12	31.7	1 40	130	181	.72	60	15.0
N 9	Dec. 14	31.4	2 10	123	174	.71	59	14.5
EXPERIMENT WITH FOOD.								
	1910.	*kilos.*	*hr. min.*	*c.c.*	*c.c.*			
N 3	Dec. 2[2]	30.9	2 23	138	181	0.76	81	15.5

[1] About 1 hr. 15 min. before experiment began, subject drank a small cup of black coffee.
[2] About 1 hr. 30 min. before the experiment began, subject ate 300 gms. of cooked oatmeal.

Physical examination.—A healthy appearing girl. Greatest weight, January 1908, 60.8 kilos. without clothing; weight, April 20, 1908, 49.2 kilos. without clothing. Height, 173 cm. No acetone odor. Pupils equal and reacted to light; tongue and teeth normal. Few cervical and axillary glands. Apex of heart within nipple line; no murmurs. Nothing abnormal felt in abdomen. Knee-jerks normal. The greatest quantity of urine was approximately 5,000 c.c., just previous to April 18, 1908.

Urine data.—The course of the disease is given in table 34. Although the urine showed 4.8 per cent of sugar on April 18, 1908, it will be seen that under the restriction of the carbohydrates to approximately 10 grams the urine became sugar-free. The tolerance for carbohydrates gradually increased, and reached approximately 90 grams of carbohydrates in February 1909, where it remained until after October 28, 1909. The weight rose from 49.2 kilos., April 20, 1908, to 55.8 kilos., July 28, 1909. The health was so good that the local physician would not believe that the patient had diabetes, and allowed a free diet on Thanksgiving Day, 1909. Sugar returned early in December 1909, but disappeared at once when the diet was again restricted. A tolerance of 55

grams of carbohydrate was reached February 18, 1910, but after April 21 of that year sugar was seldom absent until the patient's death.

The reaction of the urine was acid throughout, except upon April 30, 1908. Diacetic acid was present when the patient was first seen, but disappeared when the urine became sugar-free, not returning until September 1910. The β-oxybutyric acid reached 14.3 grams upon September 23–24, 1910, but the ammonia was low, which was due in part to the sodium bicarbonate administered.

TABLE 34.—*Clinical chart—Case O.*

Date.	Volume of urine.	Specific gravity.	Diacetic acid.	β-oxybutyric acid.	Nitrogen.	Ammonia. Total	Ammonia. $\frac{NH_3-N}{Total\ N.}$	Sugar. By copper reduction.	Sugar. By rotation.	Carbohydrates in diet	$NaHCO_3$	Carbohydrate balance.	Body weight without clothing.
1908.	c.c.			gms.	gms.	gms.	p. ct.	gms.	gms.	gms.	gms.	gms.	kilos.
Apr. 18–19	1800	....	+	....	....	....	....		50	90	8	+ 40	....
Apr. 19–20	2610	1027	......	....	....	1.9	..		78	90	8	+ 10	49.2
Apr. 20–21	1710	...	++	....	....	....	...	..	44	64	8	+ 20	49.2
Apr. 21–22	1890	..	++	....	.	.	..		60	60	8	...	49.2
Apr. 22–23	1600±	....	+	...	20.1	1.9	7.8		42	60	8	+ 20	49.4
Apr. 23–24	1650	....	+	...	....	...	...	..	20	40	8	+ 20	49.5
Apr. 24–25	1650	....	+	....	.	..	.	..	17	20	8	+ 5	49.6
Apr. 25–26	1590	....	+	....	....	...	..	.	16	15	8	...	50.2
Apr. 26–27	2970	....	+	....	....	1.5	..	0	12	10	8	..	50.4
Apr. 27–28	1650	....	0	....	....	...	..	0	..	12	8	+ 10	50.0
May 1– 2	1830	....	0	....	13.0	....	....	0	.	10	0	+ 15	50.2
1910.													
Sept. 8– 9	[1] 1140	1017	0	....	....	....	....		2	....	0	..	50.9
Sept. 9–10	1830	1030	+	...	....	1.7	....		44	10	0	– 35	50.9
Sept. 10–11	2200	....	++	....	....	....	....		47	10	0	– 35	51.4
Sept. 11–12 [2]	2640	1027	+	.	20.7	....	....	..	53	10	8	– 45	51.3
Sept. 12–13	2340	1025	+	12.6	20.1	1.4	5.7		33	10	20	– 25	52.2
Sept. 13–14	1470	1025	+	...	....	....	....		12	10	20	...	52.3
Sept. 14–15	2760	1019	++	....	17.2	...	....	.	11	10	20	...	52.4
Sept. 15–16	2760	1024	++	....	15.6	..	....	32	22	10	20	– 20	52.4
Sept. 16–17	2940	1015	+++	....	18.3	0.8	3.6	47	29	10	20	– 35	51.6
Sept. 17–18 [3]	1440	1028	+++	....	8.7	0.4	3.8	27	29	145	20	+120	52.0
Sept. 18–19 [4]	2820	1023	......	....	13.6	0.5	3.0	17	11	15	20	...	53.0
Sept. 19–20 [4]	3420	1026	+++	...	12.9	....	....	43	27	15	20	– 30	52.3
Sept. 20–21	3420	1022	0	....	15.2	....	....	38	14	15	20	– 25	52.7
Sept. 21–22	2880	1025	+++	....	14.1	....	....	54	40	15	20	– 40	52.8
Sept. 22–23 [5]	3280	1021	+++	13.0	11.2	0.6	4.4	42	24	15	20	– 25	52.9
Sept. 23–24 [6]	2577	1023	+++	14.3	8.0	0.5	5.1	50	43	165	20	+115	52.3
Sept. 24–25 [5]	2410	1025	+++	14.1	10.0	....	...	19	..	15	20	– 5	52.6
Sept. 25–26	3270	1022	++	....	11.1	0.9	6.7	54	39	15	20	– 40	52.3
Sept. 26–27	2460	1024	++	....	12.6	1.0	6.5	55	44	15	16	– 40	....
Oct. 3– 4	1860	1029	+++	....	....	....	....		60	20	12	– 40	52.5
Oct. 13–14	2210	1028	+++	....	14.9	2.0	11.0	62	49	....	12	...	54.2
Oct. 25–26	2300	1020	+++	....	15.9	2.4	12.4	80	64	....	..	...	53.6
Nov. 16–17	1750	1034	++++	....	....	...	...	..	49	....	..	...	...
Nov. 29–30	2000	1031	+++	.	....	...	....	+	64	....	..	..	52.6

[1] 12 hours. [2] Vegetable day. [3] Oatmeal day with 120 c.c. cream and 215 gms. butter.
[4] Vegetable day, with 240 c.c. cream. [5] Vegetable day, 240 c.c. cream, 4 eggs.
[6] Oatmeal day, 240 gms. oatmeal, 240 gms. butter, 120 c.c. cream.

EXPERIMENTS WITH CASE O.

Four respiration experiments were carried out with this subject, of varying character. The vital statistics are as follows:

Date of birth, August 16, 1894; height, 173 cm.; range in body-weight without clothing during experiments, 52.3 to 52.8 kilos.

RESPIRATION EXPERIMENT No. O1.

Date, September 22, 1910. Body-weight without clothing, 52.8 kilos.

On the day of the experiment the subject reached the laboratory, fasting, at 8h 05m a.m., and lay down on the couch immediately after the pneumograph had been adjusted. The stethoscope was not used in this experiment, the pulse-

rate being counted at the wrist. The experiment began at 8ʰ 23ᵐ a. m., continuing for three periods of 11 to 13 minutes, with intermissions of 10 to 17 minutes, ending at 9ʰ 26ᵐ a. m. The subject remained quiet throughout all three periods, except for raising her hand to her head once in the first period. The surgeon's plaster was not used to close the mouth, nor did it appear to be necessary. The subject urinated at 7 a. m., and again after the experiment at 9ʰ 30ᵐ a. m. The results are given in tables 35 and 39.

TABLE 35.—*Results of respiration experiment No. O 1.*

Date and time.	Duration.	Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration rate.
Sept. 22, 1910:	*min. sec.*	*c.c.*	*c.c.*			
$8^h\ 23^m$ a.m....	12 51	167	231	0.73	62	17
8 53 a.m...	12 29	165	219	.75	63	18
9 15 a.m...	10 36	167	228	.73	68	18
Average......	....	[1] 166	[1] 226	0.74	64	18

[1] Carbon dioxide eliminated per kilogram per minute, 3.14 c.c.; oxygen absorbed per kilogram per minute, 4.28 c.c.

RESPIRATION EXPERIMENT NO. O 2.

Date, September 22, 1910. Body-weight without clothing, 52.8 kilos.

This experiment was carried out in the afternoon of the day on which experiment No. O 1 was made, after food had been taken. The diet for this day was that of a regular vegetable day, with the addition of 4 eggs and one-half pint of cream. The subject arrived at the laboratory at about 3 p. m., and immediately lay down upon the couch. The experiment began at 3ʰ 12ᵐ p.m., continued for three periods 11 to 12 minutes in length, with the usual intermissions, and ended at 4ʰ 16ᵐ p. m. During the second period, some difficulty was experienced in obtaining a record of the pulse-rate. The subject was extremely quiet throughout the whole experiment. The records are given in tables 36 and 39.

TABLE 36.—*Results of respiration experiment No. O 2.*

Date and time.	Duration.	Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration rate.
Sept. 22, 1910:	*min. sec.*	*c.c.*	*c.c.*			
[1] $3^h\ 12^m$ p.m....	12 2	208	284	0.73	64	21
3 39 p.m....	12 3	213	299	.71	[2] 72	17
4 06 p.m....	10 5	197	267	.74	69	19
Average......	....	[3] 206	[3] 283	0.73	..	19

[1] The subject had probably taken food before this experiment. [2] One record at $3^h\ 47^m$ p.m.
[3] Carbon dioxide eliminated per kilogram per minute, 3.90 c.c.; oxygen absorbed per kilogram per minute, 5.36 c.c.

RESPIRATION EXPERIMENT NO. O 3.

Date, September 23, 1910. Body-weight without clothing, 52.3 kilos.

The experiment was made on an oatmeal day, the first being a fasting period, and the second period following an oatmeal breakfast. The subject then returned to the hospital, but after a dinner containing oatmeal, came back to the laboratory and two additional periods followed. The experiment was concluded by two periods after the subject had been again to the hospital and eaten a lunch containing oatmeal.

In the morning she reached the laboratory at 7ʰ 55ᵐ a. m., without breakfast, and lay on the couch about 10 minutes before the experiment began at

8^h 15^m a. m. There was but one 15-minute period at this time, the subject lying very quietly throughout.

Immediately after the fasting period was over, she was given oatmeal, which was eaten between 8^h 45^m a. m. and 8^h 53^m a. m. She again lay down upon the couch at 9^h 46^m a. m.; the next period began at 10^h 01^m a. m., continuing for 15 minutes. The subject was very quiet throughout the period.

At 2 p. m. the subject returned from the hospital, and immediately on her arrival at the laboratory lay down upon the couch. The measurements were begun at 2^h 15^m p. m., continuing for two periods, 10 and 12 minutes long, respectively, with an intermission of 15 minutes. No blanket was used to cover the subject, as she seemed comfortable without it.

For the later periods, the subject came to the laboratory at 5^h 30^m p. m., and the measurements began at 5^h 38^m p. m., continuing for two periods of 12 and 13 minutes each, with an intermission of 10 minutes. As in the previous periods, the subject lay very quietly.

The results of the measurements are given in tables 37 and 39.

TABLE 37.—*Results of respiration experiment No. O 3.*

Date and time	Duration.	Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration rate.
Sept. 23, 1910.	*min. sec.*	*c.c.*	*c.c.*			
Without food—						
8^h 15^m a.m. . .	14 45	[1] 165	[1] 232	0.71	60	18
After oatmeal—[2]						
10^h 01^m a.m. .	15 1	175	235	.74	66	18
2 15 p.m. .	11 55	175	257	.68	64	17
2 42 p.m. . .	10 9	180	254	.71	68	17
5 38 p.m. . .	12 9	183	262	.70	72	16
6 00 p.m. . . .	12 45	194	276	.70	70	16
Average with food. .	. . . .	[3] 181	[3] 257	.71	68	17

[1] Carbon dioxide eliminated per kilogram per minute, without food, 3.15 c.c.; oxygen absorbed per kilogram per minute, without food, 4.44 c.c.

[2] Subject ate oatmeal between 8^h 45^m a.m. and 8^h 53^m a.m. and throughout the day. (See notes.)

[3] Carbon dioxide eliminated per kilogram per minute, with food, 3.46 c.c.; oxygen absorbed per kilogram per minute, with food, 4.91 c.c.

RESPIRATION EXPERIMENT NO. O 4.

Date, September 24, 1910. Body-weight without clothing, 52.6 kilos.

The subject arrived at the laboratory, without breakfast, at 8^h 03^m a. m., and immediately lay down upon the couch. The experiment began at 8^h 17^m a. m., continuing for two periods of 12 and 13 minutes, with an intermission of 13 minutes. In both periods she was very quiet, only one slight movement of the hands in the second period being noted. As the subject seemed tired at the end of the second period, the experiment was discontinued. The results are given in tables 38 and 39.

TABLE 38.—*Results of respiration experiment No. O 4.*

Date and time.	Duration.	Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration rate.
Sept. 24, 1910:	*min. sec.*	*c.c.*	*c.c.*			
8^h 17^m a.m.	12 6	155	213	0.73	58	16
8 42 a.m.	12 42	149	209	.71	60	16
Average.	. . . .	[1] 152	[1] 211	.72	59	16

[1] Carbon dioxide eliminated per kilogram per minute, 2.89 c.c.; oxygen absorbed per kilogram per minute, 4.01 c.c.

TABLE 39.—*Statistics of urine—Respiration experiments Nos. O 1–O 4.*

Date and period.	Volume.	Specific gravity.	Total nitrogen.	Sugar.
Sept. 22, 1910:	*c.c*		*gms.*	*gms.*
$7^h 00^m$ a.m. to $9^h 30^m$ a.m. . .	520	1.010	0.91	4.2
9 30 a.m. 10 00 a.m. . .	165	1.024	.62	2.5
10 00 a.m. 12 noon	600	1.019	1.64	7.8
12 00 noon 3 00 p.m.[1]	240	1.025	.74	4.1
3 00 p.m. 6 00 p.m. . . .	300	1.029	1.33	3.4
6 00 p.m. 8 15 p.m.	315	1.029	1.27	3.4
8 15 p.m. 11 45 p.m. . .	390	1.031	1.87	5.7
Sept. 22–23, 1910:				
$11^h 45^m$ p.m. to $7^h 00^m$ a.m.	750	1.024	3.00	11.0
Sept. 23, 1910:				
$7^h 00^m$ a.m. to $9^h 10^m$ a.m.[2]	432	1.016	1.08	5.9
9 10 a.m. 11 30 a.m. . . .	480	1.022	1.39	9.3
11 30 a.m. 4 00 p.m. . . .	420	1.018	1.21	6.3
4 00 p.m. 7 15 p.m.	330	1.027	1.04	6.4
7 15 p.m. 9 20 p.m.	285	1.026	.79	5.6
Sept. 23–24, 1910:				
$9^h 20^m$ p.m. to $2^h 15^m$ a.m. . .	420	1.034	1.49	8.3
Sept. 24, 1910:				
$2^h 15^m$ a.m. to $7^h 00^m$ a.m.	210	1.035	1.05	4.1
7 00 a.m. to 7 00 p.m. . .	1250	1.025	5.08	5.9
Sept. 24–25, 1910:				
$7^h 00^m$ p.m. to $7^h 00^m$ a.m.	1162	1.023	4.89	[3]13.1

[1] Food was probably eaten at about noon.
[2] Oatmeal was eaten between $8^h 45^m$ a.m. and $8^h 53^m$ a.m. and throughout the day.
[3] Sugar by fermentation.

CASE P.

DESCRIPTION OF THE CASE.

Male; born May 10, 1894; single; no occupation; lost strength in December 1910; came under our observation September 1911; diagnosis of diabetes, which was confirmed by his physician, in January 1911; died in coma November 5, 1911.

Family history.—Father and one sister well; mother in poor health; one sister died at 2 months, cause unknown. No history of diabetes in the family.

Past history.—Measles. Always good health. As the family moved frequently from place to place he was much retarded in his studies at school; this caused him much anxiety, and he consequently worked very hard.

General history of the case.—In December 1910, at the age of 17, his health failed, and the disease was diagnosed as diabetes in January 1911. He suffered from numerous furuncles which did not yield to local treatment, or treatment with vaccines. Worn out by these, the patient gradually failed, and succumbed to coma on November 5, 1911.

Physical examination.—Greatest weight, 49.9 kilos.; usual weight, 48.6 kilos.; January 1911, 45.8 kilos.; September 16, 1911, 42.1 kilos.; all weights without clothing. Height, 173 cm. Acetone odor to breath. Examination negative except for numerous furuncles, especially about the neck.

Urine data.—The quantity of urine in January 1911 was approximately 5,000 c.c. The sugar disappeared after treatment for a month, but then permanently returned. The reaction of the urine was acid throughout the period of observation. The ammonia amounted to 3.3 grams shortly after the patient came under observation in September 1911, rising to 6.5 grams October 14–15. The acidosis was so considerable that no great restriction of diet was attempted. The albumen never exceeded a very slight trace. The urinary record is given in table 40.

EXPERIMENTS WITH CASE P.

With this subject, three bed-calorimeter experiments were made and eight respiration experiments; the larger part of these formed a part of two series. Series I, which was made on September 29, 1911, consisted of three experiments, *i.e.*, a respiration experiment (P 2), followed by an experiment with the bed calorimeter (P 3), and concluded by a second respiration experiment (P 4). Series II, which was carried out October 9–10, 1911, included five experiments, beginning with a respiration experiment (P 5) with the subject fasting, which was followed by two oatmeal experiments, the first with the bed calorimeter

TABLE 40.—*Clinical chart—Case P.*

Date.	Volume of urine.	Specific gravity.	Diacetic acid.	Nitrogen.	Ammonia. Total.	Ammonia. NH₃—N / Total N.	Sugar. By copper reduction.	Sugar. By rotation.	Carbohydrates in diet.	Carbohydrate balance.	$NaHCO_3$	Body-weight without clothes.
1911	*c.c.*			*gms.*	*gms.*	*p. ct.*	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*kilos.*
Sept. 16–17	....	1033	+	....		....	...	[1]4.8	.	..	0	42.1
Sept. 17–18	3360+	1030	+	....	..	....	...	[1]4.0	85	..	0	42.1
Sept. 18–19	1920+	1028	+	....	..	....	15	[1]4.0	85	..	0	41.5
Sept. 19–20	3430	1027	Sl.+	...	...	....	144	130	100	− 45	8	40.9
Sept. 20–21	3360	1026	+	....	...	....	...	94	80	− 15	12	40.9
Sept. 21–22	2200	1027	++	....	3.3	...	86	75	75	− 10	12	40.2
Sept. 22–23	3000	1027	++	....	...	....	108	90	75	− 35	12	40.8
Sept. 23–24	2780	1025	....	...	.	....	...	61	55	− 5	12	41.1
Sept. 24–25	2980	1021	++++	13.1	4.5	28.3	75	54	45	− 30	12	40.9
Sept. 25–26	2980	1027	++++	14.5	4.6	26.1	96	78	40	− 55	12	41.3
Sept. 26–27	3090	1025	+++	....	4.4	....	105	74	40	− 65	12	40.9
Sept. 27–28	2880	1024	++	12.4	...	....	81	63	40	− 40	12	39.9
Sept. 28–29[2]	3280	1022	++++	10.9	4.9	37.0	59	39	15	− 45	20	39.7
Sept. 29–30[3]	1840	1034	0	5.3	.	....	65	55	165	+100	20	39.1
Sept. 30 to Oct. 1	3650	1023	+++	10.6	4.2	32.6	117	88	80	− 35	24	38.6
Oct. 1– 2	3600	1025	++++	14.4	4.5	25.7	78	101	80	.	24	39.5
Oct. 2– 3	4080	1026	++++	18.4	.	..	117	106	80	− 35	24	40.5
Oct. 3– 4	4000	1025	++++	16.9	...	.	120	112	80	− 40	24	40.5
Oct. 4– 5	3320+	1027	++++	14.9	...	....	[1]3.8	[1]3.0	60	.	24	40.8
Oct. 5– 6	4080	1026	++	..	4.4	....	163	139	60	−105	20	40.7
Oct. 6– 7	4360	1021	+++	13.2	2.1	13.1	48	44	50	+ 2	20	41.4
Oct. 7– 8	4500	1026	+++	17.8	5.0	23.1	99	63	50	− 50	20	41.1
Oct. 8– 9	3620	1034	++	11.1	4.1	30.4	54	36	15	− 40	16	40.0
Oct. 9–10	2835	1024	++	8.2			79	62	..		20	
Oct. 10–11	3380	1028	Sl.+	16.0	4.9	25.2	95	74	25	− 70	20	39.5
Oct. 11–12	3200	1026	++++	14.2	4.2	24.3	115	83	45	− 70	20	39.5
Oct. 12–13	3680	1024	++++	14.9	4.7	25.9	114	88	40	− 75	24	39.6
Oct. 13–14	3800	1024	+++	14.0	4.5	26.4	114	84	50	− 65	20	39.9
Oct. 14–15	4320	1026	+++	22.4	6.5	23.9	112	86	44	− 70	20	39.1
Oct. 15–16	4000	1027	++++	17.7	5.5	25.6	116	104	55	− 60	20	39.1
Oct. 16–17	2885	1032	++++	16.1	5.0	25.5	84	69	50	− 35	16	38.4
Oct. 17–18	3100	1029	++++	13.6	4.5	27.2	127	105	80	− 45	24	38.9
Oct. 18–19	3520	1027	+++++	19.5	4.7	19.8	141	113	80	− 60	20	39.4
Oct. 19–20	3380	1026	++	15.8	5.3	27.6	91	68	75	− 15	20	39.5
Oct. 20–21	4100	1022	+++	15.4	4.0	21.4	127	107	80	− 45	20	39.4
Oct. 21–22	4520	1025	++++	22.0	...	...	119	127	75	− 75	20	39.3
Oct. 22–23	3420	1024	+	14.2	4.1	23.7	116	96	75	− 40	20	38.9
Oct. 23–24	3220	1022	+++++	...	4.1	....	77	58	75	.	20	38.9
Oct. 24–25	3720	1025	.	15.2	...	....	119	.	.	.	16	39.1
Oct. 25–26	3340	...	....	17.9	..	....	97	...	..	..	12	39.1
Oct. 26–27	2800	1027	++	14.5	3.7	21.0	106	84	..	.	16	38.4

[1] Per cent. [2] Vegetable day, vegetables, bacon, broths, 240 c.c. cream.
[3] Oatmeal day, 240 gms. oatmeal, 180 gms. butter, 240 c.c. cream.

(P 6) and the other with the respiration apparatus (P 7). In the fourth experiment (P 8), the subject spent the night in the bed calorimeter, and the series was concluded by a respiration experiment (P 9) following a beefsteak breakfast. A comparison of the data for the calorimeter experiments is given in table 57. The vital statistics for this subject were as follows:

Date of birth, May 10, 1894; height, 173 cm.; range in body-weight without clothing during experiments, 38.7 to 40.9 kilos.

Respiration Experiment No. P 1.

Date, September 25, 1911. Body-weight without clothing, 40.9 kilos.

On the morning of the experiment the subject came to the laboratory, fasting, having had only a cupful of moderately strong coffee at 7 a. m. He lay down upon the couch at 7^h 32^m a. m.; mosquito netting was thrown over his face, shoulders, and arms; his feet were crossed and his arms folded upon his chest. The experiment began at 8^h 54^m a. m., continuing for three 15-minute periods, with intermissions of 14 to 17 minutes. In the first period he uncrossed his feet at 9^h 04^m a. m. In the third period he moved his arm to his side, as it felt cramped. Aside from these movements, the subject was quiet and awake throughout the experiment. Previous to the experiment, he urinated at 7 a. m., and at 8^h 30^m a.m. he urinated and defecated. The results of the experiment are given in tables 41 and 42.

Table 41.—*Results of respiration experiment No. P 1.*

Date and time.	Duration.	Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient	Average pulse-rate.	Average respiration rate.
Sept. 25, 1911:	*min. sec.*	*c.c.*	*c.c.*			
[1] 8^h 54^m a.m.	15 8	164	215	0.76	72	18
9 24 a.m	14 59	144	214	.67	72	19
9 55 a.m.	14 56	145	215	.68	69	19
Average	....	[2] 151	[2] 215	.70	71	19

[1] Subject drank a cup of coffee (quite strong) at 7 a.m.
[2] Carbon dioxide eliminated per kgm. per minute, 3.69 c.c.; oxygen absorbed per kgm. per minute, 5.26 c.c.

Table 42.—*Statistics of urine—Respiration experiment No. P 1.*

Date and period.	Volume.	Specific gravity.	Total nitrogen.	Sugar.
Sept. 25, 1911:	*c.c.*		*gms.*	*gms.*
[1] 7^h 00^m a.m. to 8^h 30^m a.m.	197	1.025	0.93	5.0
8 30 a.m. 10 14 a.m.	174	1.023	.77	3 7
Sept. 25–26, 1911:				
10^h 14^m a.m. to 7^h 00^m a.m.	2610	1.029	12.91	82.9

[1] Subject drank a cup of strong coffee at 7 a.m.

Respiration Experiment No. P 2.

Date, September 29, 1911. Body-weight without clothing, 39.7 kilos.

This was the initial experiment of Series I, and was divided into two parts, the first part following a fast, and the second following the ingestion of food.

The subject arrived at the laboratory, without breakfast, at 7^h 40^m a. m., and lay down upon the couch at 7^h 52^m a. m. At 8^h 01^m a. m. he drank a glass of water. The fasting portion of the experiment began at 8^h 20^m a. m., continued for three periods of 14 to 15 minutes, and ended at 9^h 28^m a. m. The subject then ate 375 grams of cooked oatmeal and 45.5 grams of cream, taking at the same time 4 grams of sodium bicarbonate in 100 c.c. of water, and drinking 200 c.c. of cold water. The food was taken between 9^h 42^m a. m. and 10^h 34^m a. m., although not all at one time. He urinated at 9^h 30^m a. m., and lay down on the couch again at 10^h 35^m a. m. for the final periods of the experiment; four 15-minute periods followed, beginning at 10^h 51^m a. m. and ending at 1^h 04^m p. m. He urinated at 11^h 41^m a. m. and again at 1^h 26^m p. m., after the experiment was over. The mouthpiece was used in all of the periods, the pulse and respiration rates being taken in the usual manner. After the third fasting

period the subject complained that his legs felt stiff from keeping still so long. He was awake and very quiet during practically all of the experiment, save for a few slight movements of the hands and feet which seemed to be due to nervousness. The results of the experiment are given in tables 43 and 46.

TABLE 43.—*Results of respiration experiment No. P 2.*

Date and time.	Duration.	Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration rate.
Sept. 29, 1911:						
Without food—	*min. sec.*	*c.c.*	*c.c.*			
8^h 20^m a.m.	15 0	147	205	0.72	69	17
8 46 a.m.	14 3	145	206	.70	71	17
9 13 a.m.	14 59	147	214	.69	75	19
Average.....	.	[1] 146	[1] 208	.70	72	18
With food—						
[2] 10^h 51^m a.m	14 55	177	249	71	82	19
11 16 a.m	15 4	162	228	71	80	19
12 22 p.m	14 57	162	232	70	80	19
12 50 p.m	14 45	157	227	69	77	18
Average ...	......	[3] 165	[3] 234	.70	80	19

[1] Carbon dioxide eliminated per kilogram per minute, without food, 3.68 c.c.; oxygen absorbed per kilogram per minute, without food, 5.24 c.c.
[2] Subject ate 375 gms. cooked oatmeal and 45 5 gms. cream between 9^h 42^m and 9^h 55^m a.m. and between 10^h 30^m and 10^h 34^m a.m.
[3] Carbon dioxide eliminated per kilogram per minute, with food, 4.16 c.c.; oxygen absorbed per kilogram per minute, with food, 5.89 c.c.

CALORIMETER EXPERIMENT NO. P 3.

Date, September 29, 1911. Body-weight without clothing, 39.7 kilos.

In this experiment, which was the second in Series I, the bed calorimeter was used for the first time with this subject. Food had been taken during one of the intermissions in the respiration experiment which preceded the calorimeter experiment. At 1^h 12^m p. m., a meal consisting of 241 grams oatmeal and 37 grams of cream was eaten, together with 4 grams of sodium bicarbonate taken in 100 c.c. of water. The subject entered the bed calorimeter at 1^h 37^m p. m. and the experiment began at 2^h 20^m p. m. After two 45-minute periods, the experiment ended at 3^h 50^m p. m. Both pneumographs, also the stethoscope, were used for the regular records but during the last 20 minutes of the second period the pulse-rate could not be obtained, as the subject had turned over on his side. He had boils on the back of his neck, but said after the experiment that he was very comfortable in the calorimeter, and, in fact, slept the greater part of the time. He urinated at 1^h 26^m p. m. and 3^h 55^m p. m. No water was taken during the experiment. The records of the experiment may be found in tables 44 and 46.

TABLE 44.—*Measurements of metabolism—Calorimeter experiment No. P 3.*

Date and period.	Carbon dioxide eliminated.		Oxygen absorbed.		Respiratory quotient.	Average pulse-rate.	Average respiration rate.
	Total.	Per minute.	Total.	Per minute.			
Sept. 29, 1911:	*gms.*	*c.c.*	*gms.*	*c.c.*			
[1] 2^h 20^m p.m. to 3^h 05^m p.m..... ..	14.0	[2] 158	14.6	227	0.70	73	18
3 05 p.m. 3 50 p.m.....	. .		15 0	233	. .	70	17
Total 1 hr. 30 min........... ..	..	...	29.6	[3] 230	...	..	

[1] Subject ate 241 gms. of cooked oatmeal and 37 gms. of cream between 1^h 12^m p.m. and 1^h 24^m p.m.
[2] Carbon dioxide eliminated per kilogram per minute, 2^h 20^m to 3^h 05^m p.m., 3.98 c.c.,
[3] Oxygen absorbed per kilogram per minute, 2^h 20^m to 3^h 50^m p.m., 5.79 c.c.

Respiration Experiment No. P4.

Date, September 29, 1911. Body-weight without clothing, 39.7 kilos.

This experiment was the third in Series I, respiration experiment P2 and calorimeter experiment P3 preceding it. Immediately after the subject had left the bed calorimeter, he ate 114 grams of oatmeal and 10.5 grams of cream between $4^h\ 02^m$ and $4^h\ 09^m$ p. m. At $4^h\ 10^m$ p. m. he lay down upon the couch.

Table 45.—*Results of respiration experiment No. P4.*

Date and time.	Duration.	Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration rate.
Sept. 29, 1911:	*min. sec.*	*c.c.*	*c.c.*			
[1] $4^h\ 36^m$ p.m....	14 59	179	241	0 74	78	19
5 03 p.m....	9 27	169	. .	....	82	19
Average	....	[2] 174	[2] 241	.74	80	19

[1] Subject ate 114 gms. oatmeal and 10.5 gms. cream between $4^h\ 02^m$ and $4^h\ 09^m$ p.m.

[2] Carbon dioxide eliminated per kilogram per minute, 4.38 c.c.; oxygen absorbed per kilogram per minute, 6.07 c.c.

At $4^h\ 26^m$ p. m. he took 4 grams of sodium bicarbonate in 100 c.c. of water. The experiment began at $4^h\ 36^m$ p. m., continuing for two periods of 15 and 9 minutes respectively, ending at $5^h\ 12^m$ p. m. He urinated at $3^h\ 55^m$ p. m. and $5^h\ 35^m$ p. m. The mouthpiece was used in this experiment, also, in preference to the nosepiece. The subject was reported as comfortable, very quiet, and awake. The results of the experiment are given in tables 45 and 46.

Table 46.—*Statistics of urine—Respiration experiments Nos. P2 and P4, and calorimeter experiment No. P3.*

Date and period.	Volume.	Specific gravity	Total nitrogen.	Sugar.
Sept. 29, 1911:	*c.c.*		*gms.*	*gms.*
[1] $7^h\ 00^m$ a.m. to $9^h\ 30^m$ a.m...	257	1 023	0 91	6 0
9 30 a.m. 11 41 a.m.....	255	1 024	.78	8 4
[2] 11 41 a.m. 1 26 p.m....	308	1 026	80	11 6
1 26 p.m. 3 55 p.m.....	365	1 026	.98	15 8
[3] 3 55 p.m. [4] 5 35 p.m.....	265	1 046	.67	11.0

[1] Subject ate 375 gms. of cooked oatmeal and 45.5 gms. of cream and drank 300 c.c. of water between $9^h\ 42^m$ and $10^h\ 34^m$ a.m.

[2] Subject ate 241 gms. of cooked oatmeal and 37 gms. of cream and drank 100 c.c. of water between $1^h\ 12^m$ and $1^h\ 24^m$ p.m.

[3] Subject ate 114 gms. of cooked oatmeal and 10.5 gms. of cream and drank 100 c.c. of water between $4^h\ 02^m$ and $4^h\ 09^m$ p.m.

[4] Subject ate 107 gms. of cooked oatmeal and 18.5 gms. of cream between $5^h\ 30^m$ and $5^h\ 34^m$ p.m.

Respiration Experiment No. P5.

Date, October 9, 1911. Body-weight without clothing, 40 kilos.

This was the initial experiment in Series II. The subject fasted during the experiment, having taken no food for at least 12 hours preceding it. He came to the laboratory at $7^h\ 45^m$ a. m., lay down upon the couch at $7^h\ 50^m$ a. m., and the experiment began at $8^h\ 11^m$ a. m., continuing for two 15-minute periods. The mouthpiece and noseclip were used instead of the nosepieces. The room was very warm before the experiment began, but by opening the windows a little the temperature was gradually lowered. Throughout the two periods the subject was very quiet. After it was over he complained that his mouth was dry and that he felt weak. He also said that his stomach was out of order and he was troubled by gas, but felt hungry. The records of the experiment are given in tables 47 and 52.

TABLE 47.—*Results of respiration experiment No. P5.*

Date and time.	Duration.	Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration rate.
Oct. 9, 1911:	*min. sec.*	*c.c.*	*c.c.*			
$8^h\ 11^m$ a.m.....	15 4	148	219	0.68	71	17
8 37 a.m.....	15 8	145	212	.68	77	18
Average......	....	[1] 147	[1] 216	.68	74	18

[1] Carbon dioxide eliminated per kilogram per minute, 3.67 c.c.; oxygen absorbed per kilogram per minute, 5.40 c.c.

CALORIMETER EXPERIMENT No. P6.

Date, October 9, 1911. Body-weight without clothing, 40 kilos.

This experiment was the second in Series II, following the fasting experiment P5 with the respiration apparatus. Between $9^h\ 15^m$ a. m. and $9^h\ 35^m$ a. m. the subject ate 355.7 grams of oatmeal, 52.1 grams of butter, and 49.3 grams of cream. He defecated at $9^h\ 18^m$ a.m. Before entering the bed calorimeter the subject also took 4 grams of sodium bicarbonate in about 150 c.c. of water. The stethoscope and pneumographs were used, but considerable difficulty was found in adjusting the stethoscope properly. He entered the apparatus at $9^h\ 50^m$ a. m., and the experiment began at $10^h\ 59^m$ a. m., continuing for two 45-minute periods, one 59-minute period, and one 36-minute period. During the third period he urinated at $1^h\ 15^m$ p.m. After the experiment the subject said he had been very comfortable throughout the whole time and had slept the greater part of the experiment. His statement was borne out by the records of the changes in the temperature of the calorimeter, for he was very quiet nearly all of the time. The measurements taken during the experiment are given in tables 48 and 52.

TABLE 48.—*Measurements of metabolism—Calorimeter experiment No. P6.*

Date and period.	Carbon dioxide eliminated. Total.	Carbon dioxide eliminated. Per minute.	Oxygen absorbed. Total.	Oxygen absorbed. Per minute.	Respiratory quotient.	Average pulse-rate	Average respiration rate.
Oct. 9, 1911:	*gms.*	*c.c.*	*gms.*	*c.c.*			
[1] $10^h\ 59^m$ a.m. to $11^h\ 44^m$ a.m......	15.5	174	16.1	250	0.70	77	18
11 44 a.m. 12 29 p.m	13.7	156	12.7	198	.79	79	18
12 29 p.m. 1 28 p.m......	18.4	158	20.3	242	.66	81	17
1 28 p.m. 2 04 p.m	11.5	163	9.4	183	.89	78	19
Total 3 hrs. 5 min.[2]...........	59.1	163	58.5	221	....	..	..

[1] Subject ate 355.7 gms. of cooked oatmeal, 52.1 gms. of butter, and 49.3 gms. of cream between $9^h\ 15^m$ and $9^h\ 35^m$ a.m.
[2] Carbon dioxide eliminated per kilogram per minute, 4.08 c.c.; oxygen absorbed per kilogram per minute, 5.53 c.c.

RESPIRATION EXPERIMENT No. P7.

Date, October 9, 1911. Body-weight without clothing, 40 kilos.

This experiment, which was the third in Series II, was divided into two parts, the subject taking food previous to the first and the fifth periods. After experiment P6 was over, and the subject had left the bed calorimeter, he ate between $2^h\ 10^m$ p. m. and $2^h\ 23^m$ p. m., 297 grams of oatmeal, 46 grams of cream, and 44 grams of butter. He also took 4 grams of sodium bicarbonate in about 100 c.c. of water, and drank 200 c.c. of water in addition. At $2^h\ 28^m$ p. m. he lay down upon the couch, and the mouthpiece and noseclips were adjusted. The first part of the experiment began at $2^h\ 36^m$ p. m., continued for four

periods, each from 10 to 15 minutes in length, and ended at $5^h\ 05^m$ p. m. In the first and second periods the subject thought there was a slight leak about the noseclip, especially during one of three long breaths taken in the second period. He was very quiet in these two periods, except for adjusting the noseclip in the first minute of the first period. Between the second and third periods he sat up between $3^h\ 09^m$ and $3^h\ 37^m$ p. m., and drank 200 c.c. of water at $3^h\ 10^m$ p. m. He also drank 100 c.c. of water between the third and fourth periods, at $4^h\ 47^m$ p. m. In this intermission he slept most of the time. At the close of the fourth period he had a slight headache.

Before the second part of the experiment, the subject ate at $5^h\ 40^m$ p. m. 141.1 grams of oatmeal, 10.9 grams of butter, and 23.4 grams of cream. He also drank 100 c.c. of water. At 6 p. m. he defecated, and at $6^h\ 10^m$ p. m. he took 4 grams of sodium bicarbonate in 100 c.c. of water. At $6^h\ 15^m$ p. m. he drank 200 c.c. of water. He lay down upon the couch again at $6^h\ 26^m$ p. m., and four additional 15-minute periods followed, the first beginning at $6^h\ 44^m$ p. m., and the fourth ending at $9^h\ 40^m$ p. m. Between the fifth and sixth periods he sat up, but lay down again at $7^h\ 31^m$ p. m. In the intermission between the sixth and seventh periods, he urinated at $8^h\ 03^m$ p. m., and also drank 100 c.c. of water. During this period he expressed himself as being quite tired, and lay down at $8^h\ 30^m$ p. m. In the seventh period he was very quiet and awake, taking several long breaths near the end. He was reported as tired in the last period, also, and very quiet and awake. After the experiment was over he urinated and defecated at $9^h\ 50^m$ p. m. The records of the experiment are given in tables 49 and 52.

TABLE 49.—*Results of respiration experiment No. P 7.*

Date and time.	Duration.	Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration rate.
Oct. 9, 1911:	*min. sec.*	*c.c.*	*c.c.*			
[1] $2^h\ 36^m$ p.m....	10 13	181	243	0.74	83	19
2 53 p.m....	15 8	165	243	.68	88	20
[2] 3 56 p.m...	14 55	162	245	.66	84	20
4 50 p.m....	14 48	169	232	.73	86	20
Average......	....	[3] 169	[3] 241	.70	85	20
[4] $6^h\ 44^m$ p.m....	14 49	172	247	.70	74	19
7 46 p.m...	14 59	161	262	.62	73	20
8 47 p.m ...	15 3	154	230	.67	73	20
9 25 p.m....	14 59	153	230	.67	80	21
Average......	....	[5] 160	[5] 242	.67	75	20

[1] Oatmeal, 297 gms., butter, 43.6 gms., and cream, 45.7 gms., were eaten between $2^h\ 10^m$ and $2^h\ 23^m$ p.m.
[2] Subject slept most of the time between this and the following period.
[3] Carbon dioxide eliminated per kilogram per minute, 4.23 c.c.; oxygen absorbed per kilogram per minute, 6.03 c.c.
[4] Oatmeal, 141.1 gms., butter, 10.9 gms., and cream, 23.4 gms., were eaten between $5^h\ 40^m$ and $6^h\ 15^m$ p.m.
[5] Carbon dioxide eliminated per kilogram per minute, 4 c.c.; oxygen absorbed per kilogram per minute, 6.05 c.c.

CALORIMETER EXPERIMENT No. P 8.

Date, October 9–10, 1911. Body-weight without clothing, 40 kilos.

In this experiment, which was the fourth of Series II, the subject spent the night in the bed calorimeter. When the subject entered the apparatus at $10^h\ 15^m$ p. m., he was dressed in pajamas and socks, and two pillows and two blankets were given him. The stethoscope and the pneumograph about the chest were not used, but only the pneumograph about the thighs to obtain a record of the muscular movements. The measurements of the metabolism began at $11^h\ 49^m$ p. m., October 9, and continued for six periods of varying length, ending at $7^h\ 41^m$ a. m., October 10. The subject was reported as having moved in the fourth period; in the fifth period he moved about, telephoned,

urinated at 5h 48m a. m., and drank 84 c.c. of water at about 5h 30m a. m. When telephoning he reported himself as feeling well. After the experiment was over he urinated again at 7h 52m a. m. The measurements made are given in tables 50 and 52.

TABLE 50.—*Measurements of metabolism—Calorimeter experiment No. P 8.*

Date and period.	Carbon dioxide eliminated.		Oxygen absorbed.		Respiratory quotient.
	Total.	Per minute.	Total	Per minute.	
Oct. 9 and 10, 1911:	*gms.*	*c.c.*	*gms.*	*c.c.*	
[1] 11h 49m p.m. to 12h 49m a.m.	15.9	135	17.0	198	0.68
12 49 a.m. 1 49 a.m.	16.5	140	18.5	216	.65
1 49 a.m. 2 49 a.m.	16.3	138	17.3	202	.68
2 49 a.m. 4 27 a.m.	27.7	144	28.1	201	.72
4 27 a.m. 6 40 a.m.	38.7	148	41.0	216	.69
6 40 a.m. 7 41 a.m.	18.2	152	18.4	211	.72
Total 7 hrs. 52 min.[2]	133.3	144	140.3	208	..

[1] Subject ate oatmeal, butter, and cream between 5h 40m and 6h 15m p.m.
[2] Carbon dioxide eliminated per kilogram per minute, 3.60 c.c.; oxygen absorbed per kilogram per minute, 5.20 c.c.

RESPIRATION EXPERIMENT NO. P 9.

Date, October 10, 1911. Body-weight without clothing, 38.7 kilos.

Previous to this experiment, which concluded Series II, the subject ate a breakfast between 8h 15m a. m. and 8h 30m a. m., consisting of 168.9 grams of beefsteak, 16 grams of butter, and 2 small onions, sliced and fried crisp. He also took 4 grams of sodium bicarbonate in 100 c.c. of water, and drank in addition 250 c.c. of water. At 8h 35m a. m. he lay down upon the couch; the experiment began at 9h 05m a. m., and continued for four 15-minute periods, ending at 12h 10m p. m. In all of the periods the subject was very quiet, except for slight movements of the hands and feet. Between the first and second periods the subject lay upon the couch and read a newspaper; between the second and third periods he sat up, but lay down again about 15 minutes before the next period began; during the intermission between the third and fourth periods the subject slept. He urinated at 10h 30m a. m. and again at 12h 12m p. m. During the experiment he drank water only once, 120 c.c. at 10h 30m a. m. The records of the experiment are given in tables 51 and 52.

TABLE 51.—*Results of respiration experiment No. P 9.*

Date and time.	Duration.	Carbon dioxide eliminated per minute	Oxygen absorbed per minute	Respiratory quotient.	Average pulse-rate.	Average respiration rate.
Oct. 10, 1911:	*min. sec.*	*c.c.*	*c.c.*			
[1] 9h 05m a.m.	14 54	158	243	0.65	77	19
9 57 a.m.	14 52	166	244	.68	79	20
10 59 a.m.	14 42	169	248	.68	81	19
11 55 a.m.	14 50	172	241	.71	85	19
Average	....	[2] 166	[2] 244	.68	81	19

[1] Subject ate 168.9 gms. beefsteak, 16 gms. butter, and 2 small onions between 8h 15m and 8h 30m a.m.
[2] Carbon dioxide eliminated per kilogram per minute, 4.29 c.c.; oxygen absorbed per kilogram per minute, 6.30 c.c.

RESPIRATION EXPERIMENT NO. P 10.

Date, October 16, 1911. Body-weight without clothing, 39.1 kilos.

This experiment was divided into two sections. The first three periods were fasting, no food having been taken since the evening meal of the day

before, with the exception of 60 c.c. of black coffee at 8 a. m. The last five periods followed the ingestion of food. The subject had a slight cold on the day of the experiment.

TABLE 52.—*Statistics of urine—Respiration experiments Nos. P 5 to P 9 and calorimeter experiments Nos. P 6 and P 8.*

Date and period.	Volume.	Specific gravity.	Total nitrogen.	Sugar.
Oct 9, 1911:	*c.c.*		*gms.*	*gms.*
[1] $7^h 00^m$ a.m. to $9^h 13^m$ a.m.	280	1.020	0.92	5 2
9 13 a.m. 1 15 p.m.	480	1.023	1 41	14 6
[2] 1 15 p.m. 2 12 p.m.	144	1 023	42	4 5
2 12 p.m. 5 06 p.m.	460	1.025	1 18	14 4
5 06 p.m. 8 03 p.m.	373	1 023	84	12 2
8 03 p.m. 9 50 p.m.	256	1.025	.64	6.9
Oct. 9–10, 1911:				
[3] $9^h 50^m$ p.m. to $5^h 48^m$ a.m.	610	1.024	2 13	12 8
Oct. 10, 1911:				
$5^h 48^m$ a.m. to $7^h 52^m$ a.m.	232	1 027	84	6 1
[4] 7 52 a.m. 10 30 a.m.	350	1.019	1 00	8 6
10 30 a.m. 12 12 p.m.	270	1.022	1.01	7 6
Oct. 10–11, 1911:				
$12^h 12^m$ p.m. to $7^h 00^m$ a.m.	2760	. . . .	14.11	79 8

[1] Subject ate 355.7 gms. cooked oatmeal, 49.3 gms. cream, and 52.1 gms. butter between $9^h 15^m$ and $9^h 35^m$ a.m., and drank 150 c.c. water at 10 a.m.
[2] Subject ate 297 gms. cooked oatmeal, 45.7 gms. cream, and 43.6 gms. butter, and drank 300 c.c. of water between $2^h 10^m$ and $2^h 23^m$ p.m.
[3] Subject ate 141.1 gms. cooked oatmeal, 23.4 gms. cream, and 10.9 gms. of butter, and drank 400 c c. of water between $5^h 40^m$ and $6^h 15^m$ p.m.
[4] Subject ate 168 9 gms. beefsteak, 16 gms. butter, and 2 small onions, and drank 350 c.c. water between $8^h 15^m$ and $8^h 30^m$ a.m.

As usual with this subject, the mouthpiece and noseclip were substituted for the nosepieces. Both pneumographs were used, also the stethoscope. The subject lay down upon the couch at $8^h 17^m$ a. m. The experiment began at $8^h 48^m$ a. m., continued for three periods 12 to 15 minutes in length which ended at $9^h 48^m$ a. m. The subject then ate 301.5 grams of beefsteak and 20.8 grams of butter, finishing at $10^h 10^m$ a. m. He drank with the food 600 c.c. of water

TABLE 53.—*Results of respiration experiment No. P 10.*

Date and time.	Duration.	Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration rate.
Oct. 16, 1911:						
Without food.	*min. sec.*	*c.c.*	*c.c.*			
[1] $8^h 48^m$ a.m.	14 55	159	221	0.72	75	17
9 11 a.m.	15 3	154	217	.71	77	19
9 36 a.m.	11 35	152	219	.69	77	19
Average	. . . .	[2] 155	[2] 219	.71	76	18
With food.						
[3] $10^h 38^m$ a.m.	15 0	164	241	.68	79	19
11 28 a.m.	15 7	166	247	.67	82	19
12 22 p.m.	14 44	178	260	.68	83	19
1 00 p.m.	14 43	169	257	.66	81	17
1 31 p.m.	15 3	181	256	.71	88	20
Average	. . . .	[4] 172	[4] 252	.68	83	19

[1] Subject drank 60 c.c. of black coffee at 8 a.m.
[2] Carbon dioxide eliminated per kilogram per minute, without food, 3.96 c.c.; oxygen absorbed per kilogram per minute, without food, 5.60 c.c.
[3] Subject ate 391 5 gms beefsteak and 20.8 gms. butter between $9^h 53^m$ and $10^h 10^m$ a.m.
[4] Carbon dioxide eliminated per kilogram per minute, with food, 4.40 c.c.; oxygen absorbed per kilogram per minute, with food, 6.45 c.c.

and took 4 grams of sodium bicarbonate in about 100 c.c. of water. The next period began at $10^h 38^m$ a. m., the five 15-minute periods ending at $1^h 46^m$ p. m. The subject was very quiet throughout the experiment, only slight movements being reported. During the last three periods he said he felt rather tired; in

the seventh period he was sleepy, and the observer thought the lips dropped away from the mouthpiece and that the subject fell asleep once. He was awake in the last period, however. In the intermission between the fourth and fifth periods he lay upon the couch reading a newspaper. Between the sixth and seventh periods he left the room to telephone, and lay on the couch only about 5 minutes before the next period began. Between the seventh and eighth periods he stood up and took some water. In addition to the water taken with the food he drank one glassful at 8.25 a. m., 100 c.c. at $12^h\ 44^m$ p.m., and 100 c.c. at $1^h\ 25^m$ p.m. He urinated at 7 a.m., $9^h\ 50^m$ a.m., $12^h\ 11^m$ p. m., and $1^h\ 48^m$ p. m. The records of the experiment are given in tables 53 and 54.

TABLE 54.—*Statistics of urine—Respiration experiment No. P 10.*

Date and period.	Volume.	Specific gravity.	Total nitrogen.	Sugar.
Oct. 16, 1911:	*c.c.*		*gms.*	*gms.*
[1] $7^h\ 00^m$ a.m. to $9^h\ 50^m$	352	1.024	1.82	8.9
[2] 9 50 a.m. 12 11 p.m	282	1.025	1.54	6.2
12 11 p.m. 1 48 p.m	210	1.025	1.28	4.9
Oct. 16–17, 1911.				
$1^h\ 48^m$ p.m. to $7^h\ 00^m$ a.m	2040	.....	11.49	59.3

[1] Subject drank 60 c.c. of black coffee at 8 a.m. and 200 c.c. of water at $8^h\ 25^m$ a.m.
[2] Subject ate 301.5 gms. of beefsteak and 20.8 gms. of butter and drank 700 c.c. of water between $9^h\ 53^m$ a.m. and $10^h\ 25^m$ a.m.

RESPIRATION EXPERIMENT NO. P 11.

Date, October 25, 1911. Body-weight without clothing, 39.1 kilos.

This experiment was similar to the preceding experiment in that it was divided into two parts, the subject fasting in the first three periods, and the last periods following the taking of food. The mouthpiece and noseclips were used instead of the nosepieces. On the morning of the experiment, the subject came to the laboratory without breakfast, and lay down upon the couch at $7^h\ 35^m$ a. m. The first three 15-minute periods began at $7^h\ 59^m$ a. m.,

TABLE 55.—*Results of respiration experiment No. P 11.*

Date and time.	Duration.	Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration rate.
Oct. 25, 1911:	*min. sec.*	*c.c.*	*c.c.*			
Without food—						
$7^h\ 59^m$ a.m.	15 0	145	201	0.72	66	17
8 26 a.m.	15 5	146	202	.72	69	18
8 49 a.m.	14 59	147	210	70	71	19
Average	....	[1] 146	[1] 204	71	69	18
With food—						
$10^h\ 10^m$ a.m.[2]	14 56	149	244	61	74	16
11 16 a.m.	14 56	160	243	66	74	19
12 32 p.m.	15 15	194	265	73	76	19
1 31 p.m.	15 2	172	244	.70	74	18
Average	....	[3] 169	[3] 249	.68	75	18

[1] Carbon dioxide eliminated per kgm. per minute, without food, 3.73 c.c.; oxygen absorbed per kgm. per minute, without food, 5.22 c.c.
[2] Subject ate 284.5 gms. beefsteak, 23.3 gms. butter, and 2 small onions between $9^h\ 24^m$ and $9^h\ 41^m$ a.m.
[3] Carbon dioxide eliminated per kilogram per minute, with food, 4.32 c.c.; oxygen absorbed per kilogram per minute, with food, 6.37 c.c.

and ended at $9^h\ 04^m$ a. m. The subject then ate, between 9.24 and 9.41 a. m., 284.5 grams of beefsteak, 23.3 grams of butter, and two small onions, fried. He also took 4 grams of sodium bicarbonate in 100 c.c. of water. After eating, he lay down upon the couch at $9^h\ 43^m$ a. m., and the four succeeding periods began at $10^h\ 10^m$ a. m., ending at $1^h\ 46^m$ p. m. He was very quiet and awake

throughout all of the periods. Several slight motions were reported by the observer. The third period seemed very long to the subject. He was sleepy in the period directly following the taking of food, but did not go to sleep. In the intermission between the sixth and seventh periods he sat up for a time and

TABLE 56.—*Statistics of urine—Respiration experiment No. P 11.*

Date and period.	Volume.	Specific gravity.	Total nitrogen.	Sugar.
Oct. 25, 1911:	*c.c.*		*gms.*	*gms.*
$7^h\ 00^m$ a.m. to $10^h\ 50^m$ a.m.[1]	476	1.022	1.96	11.6
10 50 a.m. 1 00 p.m.	390	1.023	1.75	10.4
1 00 p.m. 2 45 p.m.	276	1.024	1.56	6.9
Oct. 25–26, 1911:				
$2^h\ 45^m$ p.m. to $7^h\ 00^m$ a.m.	2200	1.024	12.54	67.8

[1] Subject ate 284.5 gms. beefsteak, 23.3 gms. butter, and 2 small onions, and drank 500 c.c. water between $9^h\ 24^m$ and $9^h\ 55^m$ a.m.

said he felt quite tired. In this intermission, also, he drank a glass of water containing 4 grams of sodium bicarbonate. The subject urinated at 7 a. m., $10^h\ 50^m$ a. m., 1 p. m., and $2^h\ 45^m$ p. m. The records of the experiment are given in tables 55 and 56.

TABLE 57.—*Comparison of metabolism experiments in bed calorimeter with Case P*

EXPERIMENT WITHOUT FOOD.

Experiment No.	Date.	Weight of subject.	Length of experiment.	Per minute. Carbon dioxide eliminated.	Per minute. Oxygen absorbed.	Respiratory quotient.	Average pulse per minute.	Average respiration per minute.
	1911.	*kilos.*	*hrs. min.*	*c.c.*	*c.c.*			
P 8	Oct. 9–10[1]	40.0	7 52	144	208	0.69		....
EXPERIMENTS WITH FOOD.								
	1911.	*kilos.*	*hrs. min.*	*c.c.*	*c.c.*			
P 3	Sept. 29[2]	39.7	1 30	[3]158	230	[3]0.70	72	17.5
P 6	Oct. 9[4]	40.0	3 05	163	221	.73	79	18.0

[1] About 6 hours before the beginning of the experiment the subject ate 141.1 gms. cooked oatmeal, 23.4 gms. cream, and 10.9 gms. butter.
[2] About 1 hour before beginning of experiment the subject ate 241 gms. cooked oatmeal and 37 gms. cream.
[3] The carbon dioxide eliminated and the respiratory quotient for this experiment are for the period $2^h\ 20^m$ to $3^h\ 05^m$ p.m.
[4] About 1 hour 30 minutes before the experiment began the subject ate 355.7 gms. cooked oatmeal, 52.1 gms. butter, and 49.3 gms. cream.

CASE Q.

DESCRIPTION OF THE CASE.

Male; born March 1, 1896; single; no occupation; developed symptoms of diabetes at the age of 13, September 1909; came under our observation November 1910; diagnosed as diabetes January 1910; died in coma March 14, 1911.

Family history.—No history of diabetes in the family. Father, mother, and one brother well.

Past history.—Greatest weight, 54.0 kilos. without clothes; weight November 13, 1910, 51.6 kilos. without clothes. Measles, mumps, whooping-cough, severe tonsilitis in 1907.

General history of the case.—Symptoms of diabetes were first observed in September 1909. A single specimen of urine voided on rising in August 1909 was free from sugar. In November 1909 a sticky deposit was observed about the urinal, but diabetes was not proved present until January 1910. The con-

dition of the patient while at the hospital in November 1910 was critical. From December 28, 1910, to March 1, 1911, he was under the care of Dr. A. J. Hodgson, at Waukesha, Wisconsin, where he gained in weight up to 54.9 kilos. without clothing. The treatment was said to have consisted of a large quantity of vegetables, nuts, and water. Unfortunately no analysis of a specimen of the 24-hour quantity of urine was made during this period. Death occurred in coma March 14, 1911. An examination of the organs of the patient was made by Prof. F. B. Mallory, of the Harvard Medical School, who writes that it showed absolutely nothing abnormal; the pancreas was in all respects normal.

Physical examination.—A well-developed and nourished boy with good color. Height 168 cm. Pupils equal and reacted to light. Knee-jerks normal. No edema. High-arched palate. Pulse-rate 96. Physical examination was otherwise negative in September 1910.

Urine data.—The urinary record is given in table 58. Previous to November 1910, when the patient first came under observation, the greatest quantity of urine was 3000 c.c. It subsequently rose to 3500 c.c. on December 15, 1910, but after that date there is no accurate record. The reaction of the urine was acid during this period. The ammonia reached 6.4 grams on December 15, 1910, and on November 18–19, 1910, the quantity of β-oxybutyric acid was 30 grams. The albumen never exceeded a very slight trace. During the summer of 1910, the patient was sugar-free for several months. Throughout the period of observation, 20 grams of sodium bicarbonate were given the patient each day.

TABLE 58.—*Clinical chart—Case Q.*

Date.	Volume of urine.	Specific gravity.	Diacetic acid.	β-oxybutyric acid.	Nitrogen.	Ammonia. Total.	Ammonia. $\frac{NH_3-N}{Total\ N}$	Sugar By copper reduction.	Sugar By rotation	Carbohydrates in diet [6]	Carbohydrate balance	Body-weight without clothing.
1910.	c.c.			gms.	gms.	gms.	p. ct.	gms.	gms.	gms.	gms.	kilos.
Nov. 12-13.	[3]3030	1036	+++	....	....	...	.		121	.		51.6
Nov. 13-14.	3090	1032	++++	....	20.2	. .		105	93	55	−50	52 5
Nov. 14-15.	3260	1029	++	. . .	18.7	3 9	17 2	..	75	55	−20	52 1
Nov. 15-16.	3200	1032	++++		17.0			104	90	55	−50	51 5
Nov. 16-17.	2200	1034	++++		16.6	4 8	23 8	83	70	55	− 3	51.3
Nov. 17-18.	2620	1034	++++	25 4	18.1				94	55	−40	51.1
Nov. 18-19.	2820	1033	+++	30 0	15.6	5 2	27 4	111	96	55	−55	51.6
Nov. 19-20.	**2570**	**1027**	+++	**27.5**	**14.0**	**4.6**	**27.0**	**67**	**51**	**55**	**−10**	**51.4**
Nov. 20-21 [2].	2520	1029	+++	26.7	11.2	4 0	29 4	73	60	55	−20	51.4
Nov. 21-22 [4]	**1430**	**1037**	++ +++	**19 7**	**7 0**	**3.0**	**35.3**	**69**	**63**	**165**	**+95**	**61.5**
Nov. 22-23 [4]	**1565**	**1038**	+++++	**19.6**	**7.0**	**2.2**	**25.9**	**92**	**81**	**165**	**+75**	
Nov. 23-24 [5] ..	....		......	....	....	. . .	...	.	...			
Nov 24-25 ..	2250	1033	+	.	12.3			90	81	20	−70	
Nov 25-26 ..	3500	1030	+++	. . .	13 7			117	105			
Dec. 14-15 ..	3500	1035	++		....	6 4		.	140	.		.

[1] For 20 hours. [2] Vegetable day, vegetables, 6 eggs, 240 c c. cream, bacon, coffee, broths
[3] For 24½ hrs.; oatmeal day [4] Oatmeal day. [5] For record of urine for Nov. 23-24, see table 63.
[6] $NaHCO_3$ given each day, 20 gms.

EXPERIMENTS WITH CASE Q.

Four calorimeter experiments were made with this subject, all with the bed calorimeter. In the first and fourth experiments, the metabolism after a 12-hour fast was studied, and in the second and third experiments, after the ingestion of oatmeal. A comparison of the results of these experiments is made in table 64. There were no respiration experiments with this subject. The vital statistics were as follows:

Date of birth, March 1, 1896; height, 168 cm.; range in body-weight without clothing during experiments, 51.4 to 52.0 kilos.

Calorimeter Experiment No. Q 1.

Date, November 19, 1910; body-weight without clothing, 51.4 kilos.

The subject came to the laboratory early in the morning without breakfast and entered the bed calorimeter at 7ʰ 10ᵐ a. m. The experiment began at 8ʰ 09ᵐ a. m., and continued for three 45-minute periods, ending at 10ʰ 24ᵐ a. m. The pulse and respiration rates were obtained in the usual way. Throughout the whole experiment the subject lay on his back, reading, and was very quiet. After the experiment was over he said that although he felt rather warm he was very comfortable and found his stay in the chamber pleasant. The records of the experiment may be found in table 59.

Table 59.—*Measurements of metabolism—Calorimeter experiment No. Q 1.*

Date and period.	Carbon dioxide eliminated.		Oxygen absorbed.		Respiratory quotient.	Average pulse-rate.	Average respiration rate
	Total.	Per minute.	Total.	Per minute.			
Nov. 19, 1910:	*gms.*	*c.c.*	*gms.*	*c.c.*			
$8^h\ 09^m$ a.m. to $8^h\ 54^m$ a.m	16.4	184	15.5	241	0.77	79	23
8 54 a.m 9 39 a.m..	15.4	174	15.5	241	.72	79	20
9 39 a.m. 10 24 a.m . ..	14.9	169	13.8	216	.78	79	19
Total 2 hrs 15 mins.[1] . .	46.7	176	44.8	232	....		

[1] Carbon dioxide eliminated per kilogram per minute, 3.42 c.c.; oxygen absorbed per kilogram per minute, 4.51 c.c. The urine collected between $6^h\ 45^m$ and $10^h\ 40^m$ a.m. amounted to 270 c.c; specific gravity 1.029, and contained 1.75 gms. nitrogen and 8 gms. sugar.

Calorimeter Experiment No. Q 2.

Date, November 21, 1910. Body-weight without clothing, 51.5 kilos.

Previous to coming to the laboratory at 7 a. m. the subject ate a breakfast consisting of approximately 60 gms. oatmeal (weight uncooked) and 90 gms. cream. He entered the bed calorimeter at 7ʰ 20ᵐ a.m.; the experiment began at 8ʰ 18ᵐ a. m., and continued for three 45-minute periods, ending at 10ʰ 33ᵐ a. m. The subject was dressed in his ordinary clothing, and lay on a pneumatic mattress, with his head resting upon two pillows and lifted to an angle of 35° by means of a wooden head-rest. Throughout the experiment he lay very quiet on his back, without reading. Just before entering the calorimeter the subject drank water, but no water was taken during the experiment. He urinated at 6ʰ 50ᵐ a. m., before coming to the laboratory, and again at 10ʰ 51ᵐ a. m., after the experiment was over. The records are given in tables 60 and 63.

Table 60.—*Measurements of metabolism—Calorimeter experiment No. Q 2.*

Date and period.	Carbon dioxide eliminated.		Oxygen absorbed.		Respiratory quotient.	Average pulse-rate.	Average respiration rate.
	Total.	Per minute.	Total.	Per minute.			
Nov. 21, 1910:	*gms.*	*c.c.*	*gms.*	*c.c.*			
[1] $8^h\ 18^m$ a.m. to $9^h\ 03^m$ a.m....	17.6	199	14.8	230	0.86	81	18
9 03 a.m. 9 48 a.m .	17.0	192	15.9	248	.78	82	26
9 48 a.m. 10 33 a.m . .	16.4	186	15.9	247	.75	83	30
Total 2 hrs 15 min.[2]	51.0	192	46.6	242	..		..

[1] Subject ate for breakfast at about $6^h\ 30^m$ (?) a.m. approximately 60 gms. oatmeal (weight uncooked) and 90 gms. cream.

[2] Carbon dioxide eliminated per kilogram per minute, 3.73 c.c; oxygen absorbed per kilogram per minute, 4.70 c.c.

Calorimeter Experiment No. Q 3.

Date, November 22, 1910. Body-weight without clothing, 51.8 kilos.

This experiment also followed the ingestion of oatmeal, the subject eating a breakfast consisting of approximately 70 gms. of oatmeal (weight uncooked), 15 gms. butter, and 60 gms. cream. The subject reached the laboratory at $7^h\,35^m$ a. m., entered the bed calorimeter at $7^h\,46^m$ a. m., and the experiment began at $8^h\,26^m$ a. m., continuing for three 45-minute periods and ending at $10^h\,45^m$ a. m. The subject was very quiet during the first two periods, and was probably asleep during the second period. At the beginning of the third period he began reading and continued to read until shortly before the close of the experiment. The subject urinated both before and after the experiment, at $7^h\,20^m$ a. m. and $11^h\,05^m$ a. m. respectively. The records are given in tables 61 and 63.

TABLE 61.—*Measurements of metabolism—Calorimeter experiment No. Q 3.*

Date and period.	Carbon dioxide eliminated.		Oxygen absorbed.		Respiratory quotient.	Average pulse-rate.	Average respiration rate.
	Total.	Per minute.	Total.	Per minute.			
Nov. 22, 1910:	*gms.*	*c.c.*	*gms.*	*c.c.*			
[1] $8^h\,26^m$ a.m. to $9^h\,12^m$ a.m. . . .	16.3	179	15.5	235	0.76	70	23
9 12 a.m. 9 57 a.m.	15.9	180	14.3	222	.81	68	22
9 57 a.m. 10 45 a.m.	16.7	178	15.9	232	.77	66	26
Total 2 hrs. 19 min.[2]	48.9	179	45.7	230	. . . .		. .

[1] Subject ate for breakfast at about 7 (?) a. m. approximately 70 gms. oatmeal (weight uncooked), 15 gms. butter, and 60 gms. cream.
[2] Carbon dioxide eliminated per kilogram per minute, 3.46 c.c.; oxygen absorbed per kilogram per minute, 4.44 c.c.

Calorimeter Experiment No. Q 4.

Date, November 23, 1910. Body-weight without clothing, 52.0 kilos.

On the morning of the experiment the subject came to the laboratory without breakfast at $7^h\,35^m$ a. m., and entered the bed calorimeter at $7^h\,42^m$ a. m. The experiment began at $8^h\,35^m$ a. m., and continued for three 45-minute periods, ending at $10^h\,50^m$ a. m. Throughout the experiment the subject was very quiet, not even reading. He urinated both before and after the experiment, at $7^h\,25^m$ a. m. and $11^h\,03^m$ a. m., respectively. The records of the experiment are given in tables 62 and 63.

TABLE 62.—*Measurements of metabolism—Calorimeter experiment No. Q 4.*

Date and period.	Carbon dioxide eliminated.		Oxygen absorbed.		Respiratory quotient.	Average pulse-rate.	Average respiration rate.
	Total.	Per minute.	Total.	Per minute.			
Nov. 23, 1910:	*gms.*	*c.c.*	*gms.*	*c.c.*			
$8^h\,35^m$ a.m. to $9^h\,20^m$ a.m.	15.3	173	13.7	213	0.81	[1]63	30
9 20 a.m. 10 05 a.m.	15.7	178	15.3	238	.75	66	28
10 05 a.m. 10 50 a.m.	14.3	162	13.5	210	.77	65	31
Total 2 hrs. 15 min.[2]	45.3	171	42.5	220	. . . .	. .	

[1] One record at $9^h\,18^m$ a.m.
[2] Carbon dioxide eliminated per kilogram per minute, 3.29 c.c.; oxygen absorbed per kilogram per minute, 4.23 c.c.

TABLE 63.—*Statistics of urine—Calorimeter experiments Nos. Q 2–Q 4.*

Date and period.	Volume.	Specific gravity.	Total nitrogen.	Sugar.
	c.c.		*gms.*	*gms.*
Nov. 21, 1910: 6h 50m a.m.[1] to 10h 51m a.m.	410	1.035	1.93	27.0
Nov. 21–22, 1910: 10h 51m a.m. to 7h 20m a.m.	1020	1.038	..	[2]40.4
Nov. 22, 1910: 7h 20m a.m.[3] to 11h 05m a.m.	327	1.043	1.56	26.4
Nov. 22–23, 1910: 11h 05m a.m. to 7h 25m a.m.	1240	1.038	5.44	69.3
Nov. 23, 1910: 7h 25m a.m. to 11h 03m a.m.	116	1.041	.70	7.0
Nov. 23–24, 1910[4]	...	1.032	6.35	21.1

[1] Subject ate oatmeal at about 6h 30m (?) a.m. [2] Sugar by fermentation. [3] Subject ate oatmeal at about 7 (?) a.m.
[4] Volume of urine analyzed was 900 c.c. It could not be learned whether this was the total for the remainder of the 24 hours. The nitrogen and sugar for the total 24 hours are, therefore, not known.

TABLE 64.—*Comparison of metabolism experiments in the bed calorimeter with Case Q.*

EXPERIMENTS WITHOUT FOOD.

Experiment No.	Date.	Weight of subject.	Length of experiment.	Per minute. Carbon dioxide eliminated.	Per minute. Oxygen absorbed.	Respiratory quotient.	Average pulse per minute.	Average respiration per minute.
	1910.	*kilos.*	*hrs. min.*	*c.c.*	*c.c.*			
Q 1	Nov. 19	51.4	2 15	176	232	0.76	79	20.5
Q 4	Nov. 23	52.0	2 15	171	220	.78	65	29.5

EXPERIMENTS WITH FOOD.

Experiment No.	Date.	Weight of subject.	Length of experiment.	Carbon dioxide eliminated.	Oxygen absorbed.	Respiratory quotient.	Average pulse per minute.	Average respiration per minute.
	1910	*kilos.*	*hrs. min.*	*c.c.*	*c.c.*			
Q 2	Nov. 21[1]	51.5	2 15	192	242	0.80	82	24.5
Q 3	Nov. 22[2]	51.8	2 19	179	230	.78	68	23.5

[1] Subject ate oatmeal for breakfast about 1 hour 45 (?) minutes before experiment began.
[2] Subject ate oatmeal for breakfast about 1 hour 30 minutes (?) before experiment began.

CASE R.

DESCRIPTION OF THE CASE.

Male; born March 16, 1863; married; financier; developed symptoms of diabetes in November 1903, but the diagnosis was not made until March 21, 1904; came under our observation June 27, 1910; died of pulmonary tuberculosis March 14, 1912.

Family history.—No history of diabetes in the family. Father well at 82; mother died of arterio-sclerosis at 69. Three sisters and four children well. Seven uncles died of pulmonary tuberculosis.

Past history.—Wiry but not strong. Measles, mumps, whooping-cough, typhoid, scarlet fever, jaundice at approximately 15 years of age, malaria twice.

General history of the case.—The record of the case is given in full, because no patient has come under our observation who more carefully carried out modern dietetic treatment and also because of the extreme acidosis which disappeared with the onset of tuberculosis. In November 1903 the patient was "run down." In January 1904 he had polydipsia and was a trifle irritable. The urine of March 21, 1904, had a specific gravity 1.041, with a sugar content of 7.8 per cent. Under dietetic treatment sugar disappeared from the urine on April 15, 1904, and did not return until March 13, 1905, when the diet was somewhat relaxed. Later it again disappeared, not recurring until October 24, 1905. It was absent throughout 1906, and present at only two of 15 analyses

during 1907. On January 24, 1908, 0.3 per cent of sugar was present; in April of the same year Prof. von Noorden found difficulty in making the urine sugar-free despite vegetable days and oatmeal days, and following the patient's visit to Vienna the sugar was invariably present. Along with the gradual increase in acidosis which was first noted in 1908, the diet was gradually relaxed, and apparently each time with benefit. During the latter part of December 1911 tuberculosis appeared and the weight fell rapidly. With the appearance of the tuberculosis there was a gradual increase in the tolerance for carbohydrates and a decrease in the acidosis, a condition similar to that which occurred in Case A. Similar occurrences have been recorded by various writers. All data relating to the case from the beginning of observation, June 27, 1910, until death on March 14, 1912, can be considered absolutely reliable.

Physical examination.—Greatest weight, 66.7 kilos. without clothing; June 27, 1910, 60.5 kilos. without clothing. Height, 181 cm. Pupils equal and reacted to light. Teeth in excellent condition, undoubtedly due in part to cleansing by dentist every 6 weeks. Lungs normal. Heart, apex in mammillary line, systolic at base and apex. Blood-pressure, 126. Pulse-rate, 96. Right kidney large and palpable throughout. Liver, spleen, and left kidney not palpable. No note of abnormality of knee-jerks.

Urine data.—The reaction of the urine was acid throughout the period of our observation, but according to von Noorden's records, it had previously been alkaline several times. The acidosis was extreme from June 1910 until the last few months of life. In no other case coming under our observation has the quantity of β-oxybutyric acid been greater than with this patient, increasing to over 50 grams in March, April, August, September, November, and December 1911, the amount on Christmas Day being 54.8 grams. Although the amount of nitrogen in the diet was kept at a moderate level, the ammonia was high from the first, reaching 8 grams in February 1911, notwithstanding 20 grams of sodium bicarbonate were being taken daily. The quantity of sugar steadily rose from approximately 50 grams in June 1910 up to 200 grams in March 1911, but subsequently somewhat decreased, falling far below this in the spring of 1912, coincident with the presence of tuberculosis. A minus carbohydrate balance was present from June 1910 until the last two months of life. The body-weight slowly fell from 60.5 kilos. on June 29, 1910, to 34.5 kilos. on March 23, 1912. The urinary record is given in table 65.

EXPERIMENTS WITH CASE R.

With this subject one calorimeter experiment was made, in which the subject fasted and the bed calorimeter was used; three respiration experiments were also made, each of which was preceded by the ingestion of food. The vital statistics were as follows:

Date of birth, March 16, 1863; height, 181 cm.; range in body-weight without clothing during experiments, 55.3 to 58.2 kilos.

Respiration Experiment No. R1.

Date, August 1, 1910. Body-weight without clothing, 56.4 kilos.

This was intended to be only a trial experiment, since it was the first respiration experiment with this subject. After a breakfast consisting of 36 gms. of Quaker oats (weight uncooked), 125 c.c. of cream, 2 eggs, one-half biscuit, and 2 cupfuls of coffee containing 100 c.c. of sugarless diluted milk, also 4 grams of sodium bicarbonate in water, the subject came to the laboratory and lay down upon the couch at 9^h 50^m a. m. The experiment included but one period of 12 minutes, beginning at 9^h 55^m a. m. and ending at 10^h 07^m a. m. The pulse-rate ranged from 95 to 100, and the respiration-rate from 15 to 17. The results of the experiment are given in table 66.

TABLE 65.—*Clinical chart—Case R.*

Date.	Volume of urine.	Specific gravity.	Diacetic acid.	β-oxy-butyric acid.	Nitrogen.	Ammonia: Total.	Ammonia: $\frac{NH_3-N}{Total\ N}$	Sugar: By copper reduction	Sugar: By rotation.	Diet: Carbohydrates[1]	Diet: Alcohol	Carbohydrate balance	$NaHCO_3$.	Body-weight without clothing.	Remarks.
1908.	c.c.			gms.	gms.	gms.	p. ct.	gms.	gms.	gms.	gms.	gms.	gms.	kilos.	
Apr. 13-14	2000	1033	tr.		23.6	1.1	3.8		38	15±		−25			Strict diet.
Apr. 17-18	1600	1026	tr.						5	10		+5		63.9	Vegetable day.
Apr. 18-19	1700	1025	tr.			0.6			0	10		+10			Do.
Apr. 19-20	1650	1022	tr.		6.6				5	180±		+175		64.8	Oatmeal day
Apr. 20-21	1900	1018	0		6.4	0.3	3.9		8	180±		+170			Do.
Apr. 21-22	2000	1016	0		5.9	0.4	5.6		7	180±		+175		65.3	Do
Apr. 22-23	2900	1019	0		9.9	0.6	5.0		0						Vegetable day.
Apr. 23-24	1840	1025	+		12.3	0.7	4.7		15	10		+5		64.8	Do.
Apr. 24-25	1900	1024	+		14.1				2	10		+10		65.2	Strict diet; meat once.
Apr. 29-30	1880	1024	tr.		10.6	0.3	2.3		3	10		+5			Vegetable day.
Apr. 30 / May 1	2000	1024	+			0.5			2	10±		+10		65.4	Do.
May 6-7	1600	1036	+		12.8	0.4	2.6		46						Strict diet; meat once.
May 7-8	1600	1027	+						9	10±		0			Vegetable day.
1909.															
Jan. 2-3		1024						[2] 0.5							
Dec. 27-28		1026						[2] 9							
1910.															
June 19-20	2100	1029	++					91			0				Rarely a hyaline cast.
June 28-29	1720	1034	++	8.7	22.5	2.6	9.5	48	38	10±	0	−40	14	60.5	
July 4-5	2240	1027	+++	30.1	19.6	4.6	19.3	[3] 52	37	10	0	−40	14	58.5	Vegetables and eggs.
July 6-7	3340	1028	+++	28.9	22.5	5.7	20.8	[3] 107	73	20	0	−85	24	58.2	Strict diet; vegetables in 5-6-10 per cent groups, cream 250 c.c., half grapefruit.
July 10-11	2975	1028	++++	21.7	19.3	4.8	20.5	[3] 107	83	50	0	−55	24	58.9	Strict diet, vegetables 5-6-10 per cent, cream 250 c.c., half grapefruit, oatmeal 36 gms, peas 1 tablespoonful.
July 17-18	2960				18.8			88							
July 24-25	2780				16.5			81							
July 31 / Aug 1	2680				22.0			116							
Aug. 7-8	2630	1023	+++	28.1	15.0	2.2	12.1	90	68	55	15	−35	24	59.0	Strict diet; vegetables 5-6-10 per cent, cream 375 c.c., half grapefruit, oatmeal 36 gms., peas 1 tablespoonful.
Aug 14-15	2800				18.3			105							
Aug. 22-23	2800	1029	+++	31.9	18.5	4.5	20.0	85	67	55	15	−35	24	57.6	Strict diet, vegetables 5-6-10 per cent, cream 375 c.c., half grapefruit, oatmeal 36 gms., peas 1 tablespoonful.
Aug. 23-24	2320	1027	++++	26.1	16.7	3.8	18.7	64	46	20	15	−45	24	58.2	Vegetables, 450± gms., cream 250 c.c., 14 eggs, bacon 215 gms
Aug 24-25	3020	1021	++++	21.6	15.9	3.0	15.5	36	12	15	10	−20	24	58.1	Vegetables, broths.
Aug 25-26	3030	1027	+++	33.6	15.1	3.3	18.0	79	73	55	15	−25	24	57.4	As August 8.
Aug 28-29	2840	1032	++++	31.6	17.3	2.3	10.9	108	85	55	15	−55	24	57.9	Do.
Sept. 7-8	3760	1030	+++	32.9	20.6	4.5	18.0	122	93	70	15	−50	24	56.7	Strict diet; cream 250-375 c.c., half grapefruit, vegetables 5-6-10 per cent, peas 1 tablespoonful, oatmeal 36 gms., potato 90 gms.

For footnotes see page 50.

TABLE 65—Continued.

Date.	Volume of urine.	Specific gravity.	Diacetic acid.	β-oxy-butyric acid.	Nitrogen.	Ammonia. Total.	Ammonia. NH_3-N / Total N	Sugar. By copper reduction.	Sugar. By rotation.	Diet. Carbohydrates.[1]	Diet. Alcohol.	Carbohydrate balance	$NaHCO_3$.	Body-weight without clothing.	Remarks.
1910.	c.c.			gms.	gms.	gms.	p. ct.	gms.	gms.	gms.	gms.	gms.	gms.	kilos.	
Sept. 14-15	2560	1029	++++	32.8	16.8	4.1	20.1	63	41	20	8	−45	20	57.2	250 c.c. cream, 6 eggs, vegetables 450 gms., bacon 150 gms., claret 75 gms.
Sept. 15-16	**3250**	....	++++	**27.6**	**12.9**	..		**119**		[1]**125**	**40**	**+ 6**	**20**	**56.8**	Oatmeal 180 gms., cream 300 gms., eggs 3, brandy 60 gms., claret 90 gms., butter 262 gms.
Sept. 16-17	2900	1027	+++	38.5	11.7	4.4	30.9	69	46	20	30	−50	20	57.1	Cream 125 c.c., vegetables 500 gms., eggs 6, bacon, bouillon, much butter.
Sept. 17-18	3200	1028	++++	19.6	13.6	5.0	30.2	92	64	45	23	−45	14	56.1	Strict diet; oatmeal 36 gms., cream 375 c.c., half grapefruit, vegetables 200 gms.
Sept. 21-22	3340	1029	++++	40.7	18.4	4.2	18.8	113	80	55	23	−60	20	55.8	As August 8.
Oct. 5-6	3570	1029	+++	37.0	17.2	3.9	18.6	128	96	70	30	−60	20	55.8	Strict diet; vegetables 5-6-10 per cent groups, 1 tablespoonful 15 per cent, oatmeal 36 gms., cream 250 c.c., half grapefruit, potato, 90 gms.
Oct. 30-31	3230	1029	....	..	19.2	...		111	.	...					
Nov. 6-7	3175	1028	++++	29.3	17.4	4.2	19.9	82	70	20	30	−60	20	57.2	Vegetables, eggs 7½, bacon, cream 300 c.c.
Nov. 16-17	3825	1031	....	..	22.4	..		143			.	.			
Nov. 27-28	3680	1030	++++	42.3	18.5	6.2	27.6	132	110	70	30	−60	20	54.8	
Dec. 7-8	3500	1025	++++	42.6	15.8	5.1	26.5	77	56	20	30	−55	20	56.1	Butter, 7 eggs, vegetables, bacon, cream, alcohol.
Dec. 26-27	2800	1027	++++	26.8	14.7	2.8	15.7	64	50	20	30	−45	20	58.0	Do.
1911.															
Jan. 11-12	4130	1024	+++	39.6	17.0	4.2	20.3	74	58	20	30	−55	20	57.6	Do.
Jan. 25-26	4130	1029	+++	48.4	19.3	7.4	31.5	145	124	90	30	−55	20	...	Strict diet, vegetables, 5-6-10 per cent groups, 1 tablespoonful 15 per cent, oatmeal 36 gms., cream 300 c.c., half grapefruit, potato 90 gms., bread 30 gms.
Feb. 19-20	4500	....	+++	..	19.2	8.0	34.3	.	153	125	30	−30	20		Strict diet; vegetables 5-6-10 per cent, oatmeal 18 gms., potato 90 gms., bread 60 gms., cream 500 gms., grapefruit, half orange, bananas 45 gms., macaroni 60 gms.
Mar. 5-6	5120	1029	++		18.3	6.1	27.4	200	174	125	30	−75	20	56.3	Essentially the same.
Mar. 16-17	4380	1027	+++	52.7	19.5	7.1	29.9	180	158	125	30	−55	20		Do.
Apr. 2-3	3475	1030	++	26.3	14.8	4.4	24.5	139	111	125	30	−15	20	55.9	Do.
Apr. 26-27	4500	1028	+++	51.0	16.3	6.3	31.8	185	162	130	30	−55	20	55.7	Do.
May 10-11	3500	1028	++	42.4	13.2	5.3	33.0	158	133	125	30	−35	20		Do.
May 12-13	[6]548	..	....		**2.6**	.		**13**						**55.3**	Do.
May 28-29	4220	1026	++	49.8		6	.	186	152	125	30	−60	20	54.5	Do.
July 5-6	3150	1027	++	18.9	11.4	...			126	125	30	0	20	56.5	Do.
July 30-31	3900	1026	+++	36.2	14.1	5.1	29.8		117	125	30	+10	20	..	Do.
Aug. 9-10	....	1023	+++	.	..	...	. .	[2]2.5	[2]1.6	20	30	.	23	55.7	4 eggs, cream 375 c.c., bacon, vegetables 5-6-10 per cent.

For footnotes see page 59.

TABLE 65—Continued.

Date.	Volume of urine.	Specific gravity.	Diacetic acid.	β-oxy-butyric acid.	Nitrogen.	Ammonia.		Sugar.		Diet.		Carbohydrate balance	$NaHCO_3$.	Body-weight without clothing.	Remarks.
						Total.	NH_3-N / Total N	By copper reduction.	By rotation.	Carbohydrates.[1]	Alcohol.				
1911.	c.c.			gms.	gms.	gms.	p. ct.	gms.	gms.	gms.	gms	gms.	gms.	kilos.	
Aug. 10–11	3140	1027	++	36 3	9 8	4 8	40 3	122	94	95	30	– 25	23	55.8	Oatmeal 120 gms., cream 250 c.c., vegetables 5–6–10 per cent.
Aug. 11–12	3600	1024	++	46 7	8 7	4 7	41 4	97	86	95	30	0	13	56 3	Do.
Aug. 12–13	3510	1020	.....	51.5	8 6	4 6	44 0	46	26	20	30	– 25	27	56.2	As on August 9–10.
Aug. 16–17	3500	1029	+++	39.9	11.3	4 6	33.5	126	119	125	30	0	23	55.6	As on Feb. 19–20.
Sept. 6–7	3420	1029	+++	38.3	13 2	4 1	25 5	150	137	125	30	– 25	23	55 4	Do.
Sept. 17–18	3800	1029	++++	52 0	12.6	4.5	29 4	141	106	[6] 130	30	– 10	23	55 0	Vegetable protein only, except protein in 3 eggs and 300 c.c. cream with usual carbohydrate.
Sept. 27–28	3030	1032	+++	....	..	4 6	.	158	127	[6] 117	30	– 40	23	55.7	As on Feb. 19–20.
Sept. 28–29	2980	1031	+++	...	.	4 4	...	143	113	[6] 130	30	– 15	23	55 6	As on Sept. 17–18.
Sept 29–30	3870	1028	++++	....	....	5.2	...	155	116	[6] 130	30	– 25	23	55 2	Do.
Sept. 30 } Oct. 1 }	3800	1031	+++	. .	....	5.5	....	182	152	126	30	– 55	23	54.7	As on Feb. 19–20.
Oct. 8–9	3800	1030	++	....	...	5 5	.	190	152	135	30	– 55	23	54.6	Same, plus 10 gms. carbobydrate.
Oct. 22–23	4000	1027	++++	34.9	14.2	7 1	41 1	180	144	135	30	– 45	23	53 8	Do.
Nov. 12–13	4400	1027	++	52.0	13	5 5	34.8	198	158	135	30	– 65	23	54.3	Do.
Nov. 14–15	3800	1028	+	34.6	17	5 4	26.1	141	122	115	60	– 25	23	54.1	Butter 60 gms , oatmeal 150 gms., 2 cups broth, 600 c.c. cream = 180 gms. fat.
Nov. 15–16	3800	1028	+++	....	11.4	5.4	39.0	144	114	130	45	– 15	23	54.2	As on Sept. 17–18.
Nov. 30 } Dec. 1 }	4200	1028	++	46.2	13.4	5.2	31.9	168	151	135	45	– 35	23	53.7	As on Oct. 8–9.
Dec. 25–26	4700	1027	+++	54.8	14.5	6.3	35.7	188	160	135	45	– 55	23	50.4	Do.
1912.															
Jan 9–10	4840	1028	++	....	...	6.5	....	198	104	150	45	– 50	23	...	Same, plus 15 gms. carbohydrate.
Jan. 14–15	4000	1029	++	.. .	13.8	5.1	30 4	132	120	100	45	– 30	30	53.2	
Jan. 15–16	3860	1029	+	....	9.9	4.8	39 9	154	154	170	60	+ 15	30	....	
Jan. 17–18	4945	1024	+	...	10.8	4.5	34 3	124	109	105	60	– 20	30	53.1	
Feb. 4–5	5270	.	....	...	..	...	..			150	45	.	25	49.9	
Feb. 6–7	4820	1029	sl.+	....	17.3	5.2	24 7	198	183	150		– 50	25	....	
Feb 12–13	4864	1027	sl.+	....	16.0	6.2	31 9	184	146	100	45	– 85	25	....	
Feb 25–26	5175	1027	++	....	14.3	6.2	35 7	191	176	150	[7] 45	– 40	25	....	
Mar. 14–15.	4200 [8]	1020	0	..	9.6	. .	....	126	134	150	[7] 45	+ 25	15	....	
Mar. 17–18	2940	1020	0	6 1	9 1	0 9	8.1	82	82	150	[7] 45	+ 70	15	....	
Mar. 22–23.	2700	1026	0	6 3	12 1	...	..	135	118	150	[7] 45	+ 15	10	34.5	
Mar. 26–27	2400	1032	0	2 6	9 9	1.3	10.8	134	115	150	[7] 45	+ 15	5	....	
Apr. 2–3.	2100	1030	0	....	.	...	....	105	105	150	[7] 45	+ 45	5	....	
Apr. 7–8.	1680	1033	0	..	11 6	...	....	99	87	160	[7] 45	+ 60	5	....	

[1] Carbohydrates in diet up to June 29, 1910, are only approximately correct, but subsequent to that date are most accurate.
[2] Per cent. [3] By fermentation.
[4] Protein, 60± gms.; nitrogen, 10± gms.; fat, 345± gms.
[5] Not 24-hour urine (See statistics of urine, table 69.)
[6] 75 gms of protein Sept. 17–18, 28–29, and 29–30; 79 gms Sept. 27–28.
[7] Approximate.
[8] 22 hours.

Respiration Experiment No. R2.

Date, August 15, 1910. Body-weight without clothing, 58.2 kilos.

This experiment was preceded by the ingestion of food, and consisted of but one 14-minute period, beginning at $10^h 15^m$ a. m. The results of the experiment are given in table 66.

Table 66.—*Results of respiration experiments Nos. R1 to R3.*[1]

Experiment No.	Date and time.	Duration.	Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration rate.
	1910	*min. sec.*	*c.c.*	*c.c.*			
R 1	Aug. 1. $9^h 55^m$ a.m.	12 6	[2]227	[2]310	0.73	98	16
R 2	Aug. 15. $10^h 15^m$ a.m.	14 24	[3]224	[3]334	0.67	81	15
R 3	Sept 15. $1^h 07^m$ p.m.	11 52	207	310	.67	82	16
	1 25 p.m.	11 58	208	310	.67	83	18
	Average		[4]208	[4]310	.67	83	17

[1] Food was taken by the subject before each of these experiments.
[2] Carbon dioxide eliminated per kilogram per minute, 4.02 c.c.; oxygen absorbed per kilogram per minute, 5.50 c.c. The urine collected between $7^h 55^m$ and $10^h 25^m$ a.m. amounted to 340 c.c. and contained 2.47 gms. nitrogen and 16.5 gms. sugar.
[3] Carbon dioxide eliminated per kilogram per minute, 3.85 c.c.; oxygen absorbed per kilogram per minute, 5.74 c.c.
[4] Carbon dioxide eliminated per kilogram per minute, 3.64 c.c.; oxygen absorbed per kilogram per minute, 5.42 c.c.

Respiration Experiment No. R3.

Date, September 15, 1910. Body-weight without clothing, 57.2 kilos.

This experiment was also made after the ingestion of food and included two periods, each of 12 minutes. The subject arrived at the laboratory at $12^h 45^m$ p. m., and lay on the couch for about 10 minutes before the experiment began at $1^h 07^m$ p. m. The stethoscope was not used, the pulse-rate being counted at the wrist. The subject lay perfectly quiet throughout the whole experiment. The results are given in tables 66 and 67.

Table 67.—*Statistics of urine—Respiration experiment No. R3.*

Date and period.	Volume.	Total nitrogen.	Sugar
Sept 15, 1910.[1]	*c.c.*	*gms.*	*gms.*
$7^h 30^m$ a.m. to $10^h 00^m$ a.m.	250	1 65	9 9
10 00 a.m. 1 00 p.m.	433	1 99	19.2
1 00 p.m. 1 55 p.m.	145	65	6.6
1 55 p.m. 9 30 p.m.	1115	4.01	43.6
Sept. 15–16, 1910:			
$9^h 30^m$ p.m. to $7^h 30^m$ a.m.	1310	4 68	44.4

[1] Subject probably ate food as usual.

Calorimeter Experiment No. R4.

Date, May 12, 1911. Body-weight without clothing, 55.3 kilos.

The subject fasted in this experiment, coming to the laboratory at $7^h 20^m$ a. m., without breakfast. This was the first time the bed calorimeter had been used with this subject and, after he entered the apparatus at $7^h 51^m$ a. m., he seemed somewhat nervous and apprehensive, asked a great many questions, and moved around considerably. The experiment began at $8^h 54^m$ a. m., and continued for two periods, one of 45 minutes and the other of 47 minutes, ending at $10^h 26^m$ a. m. Especially during the first period he was more active than the average subject, telephoning, urinating, and drinking water. The pulse-rate was obtained as usual with the stethoscope, and the two pneumographs were

used to obtain records of the respiration rate and the major movements. At $9^h 20^m$ a. m. the subject drank 60 c.c. of water. After coming to the laboratory in the morning he urinated at $7^h 28^m$ a. m., also during the experiment, at $9^h 15^m$ a. m., and after the experiment was over, at $10^h 40^m$ a. m. The records are given in tables 68 and 69.

TABLE 68.—*Measurements of metabolism—Calorimeter experiment No. R4.*

Date and period.	Carbon dioxide eliminated.		Oxygen absorbed.		Respiratory quotient.	Average pulse-rate.	Average respiration rate.
	Total.	Per minute.	Total.	Per minute.			
May 12, 1911:	*gms.*	*c.c.*	*gms.*	*c.c.*			
$8^h 54^m$ a.m. to $9^h 39^m$ a.m.	17.1	193	18.2	283	0.68	70	17
9 39 a.m. 10 26 a.m.	17.9	194	17.4	260	.75	70	16
Total 1 hr. 32 min.[1]	35.0	194	35.6	271	.72	70	17

[1] Carbon dioxide eliminated per kilogram per minute, 3.51 c.c: oxygen absorbed per kilogram per minute, 4.90 c.c.

TABLE 69.—*Statistics of urine—Calorimeter experiment No. R4.*

Date and period.	Volume.	Specific gravity.	Total nitrogen.	Sugar.
May 12, 1911:	*c.c.*		*gms.*	*gms.*
$7^h 28^m$ a.m.	115	1.026	0.55	2.8
7 28 a.m. to $9^h 15^m$ a.m.	251	1.025	1.19	5.9
9 15 a.m. 10 40 a.m.	182	1.024	.87	3.9

CASE S.

DESCRIPTION OF THE CASE.

Male; born 1853; married; merchant; onset of diabetes in 1899; came under our observation May 12, 1910; died in coma October 19, 1910.

Family history.—No history of diabetes mellitus. Father died at 87; mother of cancer; one brother of liver trouble; one brother and one sister in infancy; one son 33 years old, well.

Past history.—Health neither very poor nor very good. Measles, mumps, herpes, hemorrhoids.

General history of case.—The diabetes was first apparent in 1899 with malaise. The greatest quantity of sugar noted was 3.5 per cent, while the greatest volume of urine was 2400 c.c. The general condition of the patient was excellent. The patient was under observation for only a short period of time. Death occurred some 5 months afterwards while the patient was traveling, and was considered due to coma.

Physical examination.—Greatest weight, April 1901, was 71.1 kilos. without clothes; May 13, 1910, 57.6 kilos. undressed. Height, 177 cm.; tour de taille 76 cm.; pupils equal, reacted; knee-jerk normal; blood-pressure 120; pulse 72. Nothing abnormal noted about the heart and lungs. Liver extended 2 fingers' breadth below costal margin. Spleen extended to the costal margin and was hard.

Urine data.—The urinary records of the case are given in table 70. Throughout the observation of the urine the reaction in all cases was acid, and the slightest possible trace of albumen was present on every day except May 16–17. On all days of the observation, 8 grams of sodium bicarbonate were given.

EXPERIMENTS WITH CASE S.

Two experiments were made with this subject, in both of which the respiration apparatus was used. One was a fasting experiment and the other followed the ingestion of oatmeal. The vital statistics were as follows:

Date of birth, ——, 1853; height, 177 cm.; body-weight without clothing during experiments, 58 kilos.

TABLE 70.—*Clinical chart—Case S.*

Date.	Volume of urine.	Specific gravity.	Diacetic acid.	Nitrogen.	Ammonia. Total.	Ammonia. NH_3—N / Total N	Sugar. By copper reduction.	Sugar. By rotation.	Carbohydrates in diet.[1]	Carbohydrate balance.	Body-weight without clothing.
1910.	*c.c.*			*gms.*	*gms.*	*p. ct.*	*gms.*	*gms.*	*gms.*	*gms.*	*kilos.*
May 12-13......	....	1023	0	....	.	....	..	[2]1.4	..	..	57.6
13-14......	1920	1019	Sl.+	13.1	1.5	9.4	16	8	[3]20	+ 5	57.8
14-15......	2520	1020	++	13.8	...	....	34	10	20	−15	57.7
15-16......	2400	1020	+	11.7	...	. .	39	19	15	−25	57.6
16-17......	1830	1022	Sl.+	10.6	...		38	22	20	−20	57.7
17-18......	1920	1022	+	10.4	1.6	12.7	34	19	20	−15	58.2
18-19.....	1860	1019	++	7.3	1.2	13.5	26	15	45	+20	57.9
19-20 . .	1800	1021	+	..	...	.	..	29	45	..	58.1
20-21 .	2220	1024	0	11.5	...	.	58	44	45	−15	58.3
21-22 .	1800	1021	++	8.6	...	. .	31	13	45	+15	57.9
22-23 .	1740	1023	+	9.5	...	....	36	24	45	+10	57.5

[1]8 gms. sodium bicarbonate given each day. Beginning May 13 the diet contained 200+ gms. fat and 12 gms. alcohol. [2]Per cent. [3]12± gms. nitrogen.

RESPIRATION EXPERIMENT No. S1.

Date, May 18, 1910. Body-weight without clothing, 58 kilos.

As this subject had not previously been experimented upon and was somewhat elderly, only three periods of 10 to 11 minutes were run, so as not to overtire him. The subject came from the hospital at $8^h\ 15^m$ a. m., without breakfast, and lay down upon the couch for some 10 minutes before the experiment began at $8^h\ 40^m$ a. m. Surgeon's plaster could not be used on account of his moustache and beard. The stethoscope, also the pneumographs about the chest and thighs, were used. The experiment was without incident, the subject lying quietly throughout. After the experiment was over the subject urinated at $9^h\ 45^m$ a. m. The results are given in table 71.

TABLE 71.—*Results of respiration experiment No. S1.*

Date and time.	Duration.	Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration rate.
May 18, 1910:	*min. sec.*	*c.c.*	*c.c.*			
$8^h\ 40^m$ a.m.....	11 21	148	...	....	59	8
9 03 a.m.....	10 20	154	218	0.71	58	9
9 25 a.m.....	10 9	156	208	75	57	9
Average......	....	[1]153	[1]213	.73	58	9

[1]Carbon dioxide eliminated per kilogram per minute, 2.64 c.c.; oxygen absorbed per kilogram per minute, 3.67 c.c. The urine collected between 8 and $9^h\ 40^m$ a.m. amounted to 92 c.c. and contained 0.53 gm. nitrogen and 1.9 gms. sugar.

Respiration Experiment No. S2.

Date, May 21, 1910. Body-weight without clothing, 58 kilos.

The subject came to the laboratory after eating at the hospital a breakfast of approximately 250 gms. of cooked oatmeal between $7^h 30^m$ a. m. and $7^h 45^m$ a. m. He lay down upon the couch at $8^h 10^m$ a. m., and the experiment began at $8^h 16^m$ a. m., continuing for four periods, 11 to 12 minutes long, with intermissions of 12 to 15 minutes. Both pneumographs were used. The subject urinated at $7^h 45^m$ a. m., before the experiment, and again after the experiment, at 10 a. m. The data are given in table 72.

Table 72.—*Results of respiration experiment No. S2.*

Date and time.	Duration.	Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration rate.
May 21, 1910:	*min. sec.*	*c.c.*	*c.c.*			
[1] $8^h 16^m$ a.m....	11 14	162	208	0.78	62	8
8 43 a.m....	12 5	162	223	.72	58	9
9 10 a.m....	11 41	156	212	.73	58	9
9 34 a.m....	12 21	162	213	.76	57	10
Average......	....	[2] 161	[2] 214	75	59	9

[1] Subject ate oatmeal for breakfast between $7^h 30^m$ and $7^h 45^m$ a.m.

[2] Carbon dioxide eliminated per kilogram per minute, 2.78 c.c.; oxygen absorbed per kilogram per minute, 3.69 c.c. The urine collected between $7^h 45^m$ and 10 a.m. amounted to 245 c.c. and contained 1.04 gms. nitrogen and 19.2 gms. sugar.

In order to compare his metabolism with that of a normal subject after eating oatmeal, an experiment was made with another subject who had eaten 434 gms. of cooked oatmeal. The time intervening between the ingestion of the oatmeal and the beginning of the experiment was the same as in the experiment with the diabetic. The respiratory quotients obtained with the normal subject were 0.806, 0.807, 0.854, and 0.780, respectively.

CASE T.

DESCRIPTION OF THE CASE.

Male; born 1867; married; farmer; onset of diabetes in September 1908; diagnosed November 1908; came under our observation December 5, 1910; died in coma March 5, 1911.

Family history.—No history of diabetes mellitus. Father died at 77 years of heart disease; mother at 63 years of cancer; wife and six children well; one child died of heart disease.

Past history.—Measles, mumps, whooping-cough, scarlet fever.

General history of case.—September 1908, there were polydipsia and polyuria, with loss of weight for a month previous to the diagnosis in November 1908. The chief symptom was weakness. Carbuncles and boils developed in October 1910, and the patient also suffered from constipation. The diet was at no time strict, as the feebleness of the patient, his inability to bear sodium bicarbonate well, and the severity of the acidosis made restrictions of diet appear impracticable. The patient failed to respond to diet, and died in coma March 5, 1911, shortly after returning home.

Physical examination.—Greatest weight without clothing, 71.2 kilos.; normal weight without clothing, 67.6 kilos.; weight December 5, 1910, 52.7 kilos. without clothing. Height, 180 cm. Pupils equal and reacted. Knee-jerk normal. No edema. Lungs and heart normal. Pulse-rate, 72. There were numerous boils and ulcers, some of which were partially healed, over the clavicle, neck, arms, and back—a truly pitiable sight. The breath had an acetone odor.

Urine data.—The greatest quantity of urine was 10,000 c.c. at about the time of onset. When the patient came under observation the acidosis was extreme; this is indicated by the 6 grams of ammonia shown in table 73, which gives the urinary record during observation. The reaction of the urine during this period was acid throughout, with a slight trace of albumen. The carbohydrate balance was for the most part minus throughout. Beginning January 31, 1911, 22 grams of alcohol were given daily.

TABLE 73.—*Clinical chart—Case T.*

Date.	Volume of urine.	Specific gravity.	Diacetic acid.	β-oxybutyric acid.	Nitrogen.	Ammonia. Total.	Ammonia. $\frac{NH_3-N}{Total\ N}$	Sugar. Copper reduction.	Sugar. Rotation before fermentation	Carbohydrates in diet.[1]	Carbohydrate balance	$NaHCO_3$.	Body-weight without clothing
1910.	*c.c.*			*gms.*	*gms.*	*gms.*	*p. ct.*	*gms.*	*gms.*	*gms.*	*gms.*	*gms*	*kilos.*
Dec. 4– 5	5000	1037	0	. . .	. . . .	. . .	. .	+	[2]7.2	. . .	.	.	. .
Dec. 28–29	[3]5000	1033	Sl.+	. . .	.	. . .	. . .	+	240	. . .	. .	.	. . . .
1911.													
Jan. 27–28	6000	1037	Sl.+	. . .		.	. . . .	+	408	. . .	. .		53.9
Jan. 28–29	[4]3200	1035	. . . . . .		.		. . . .	. . .	211	. . .	. .		52.7
Jan. 29–30	4500±	1037	++	.		. .	. . . .	. . .	279	195	− 85		52.4
Jan. 30–31	3400	1036	++	. .		.	. .	. .	204	200	− 5		50.9
Jan. 31–Feb. 1	4700	1031	+++	. . .	. .	. .	. . .	.	197	200	+ 5	24	50.6
Feb. 1– 2	4480	1029	+++		. . .				179	200	+ 20	30	51.7
Feb. 2– 3	5100	1030	+++	. .	.	.			204	185	− 20	30	53.2
Feb. 3– 4	5740		+++	. .	.			.	184	165	− 20	30	53.1
Feb. 4– 5	5700	1027	++						171	155	− 15	30	51.8
Feb. 5– 6	2980	1032	++			. .		146	131	140	− 5	20	50.6
Feb. 6– 7	2960	1037	++	. .	.	. . .	. .	.	178	185	+ 5	12	52.3
Feb. 7– 8	4000	1033	++	. . .	. . . .	. . .	. . . .	. . .	176	150	− 25	12	52.7
Feb. 8– 9	3420	1032	+	. . . .	. . . .	. . .	. . . .	. . .	150	140	− 10	12	52.8
Feb. 9–10	5000	1030	+	. . . .	. . .	6.0	. . . .	230	200	140	− 90	12	52.8
Feb. 10–11	4000	1033	++	. . . .	16.2	. . .	. . . .	184	168	140	− 45	12	52.4
Feb. 11–12	4380	1033	++	. . . .	18.1	. .	. . . .	219	210	140	− 80	12	53.2
Feb. 12–13	4580	1032	+++	. . . .	17.9	. .	. . . .	198	174	140	− 60	12	53.2
Feb. 13–14	4180	1031	+	43.3	13.6	5.5	33.3	179	167	140	− 40	12	52.6
Feb. 14–15	**3305**	**1032**	**++**	**40.6**	**11.6**	**5.2**	**36.9**	**138**	**119**	**130**	**− 10**	**12**	**51.5**
Feb. 15–16[5]	3335	1027	++	50.1	11.7	5.5	38.7	73	53	15	− 60	12	51.5
Feb. 16–17[6]	**3190**	**1023**	**+**	**39.7**	**9.3**	**4.6**	**40.7**	**58**	**57**	**166**	**+110**	**12**	**50.9**
Feb. 17–18	3120	1028	+++	30.2	11.0	. . .	. . . .	128	125	115	− 15	12	52.2

[1] Whisky, 45 gms. daily throughout stay in hospital. [2] Per cent.
[3] Urinary sediment contained many fine and coarse granular casts.
[4] 18 hours. Urinary sediment contained many hyaline, fine, and coarse granular casts.
[5] Vegetable day 240 c.c. cream, 4 eggs. [6] Oatmeal day, 240 gms. oatmeal, 240 gms. butter, 240 c.c. cream.

EXPERIMENTS WITH CASE T.

Two fasting experiments were made with this subject, in both of which the bed calorimeter was used. A comparison of the data obtained is made in table 76. The vital statistics were as follows:

Date of birth, 1867; height, 180 cm.; range in body-weight without clothing during experiments, 51.3 to 51.5 kilos.

CALORIMETER EXPERIMENT NO. T1.

Date, February 14, 1911. Body-weight without clothing, 51.5 kilos.

Previous to this experiment no food had been taken by the subject since the evening meal of the day before, with the exception of a cupful of coffee at $6^h\ 30^m$ a.m. When the subject arrived at the laboratory at 8 a.m. he appeared to be a very weak, sick man, and somewhat apprehensive in regard to the experiment. He was dressed in unusually warm, heavy clothing, and on entering the bed calorimeter, at $8^h\ 26^m$ a.m., was also covered with a blanket. The experiment began at $9^h\ 18^m$ a. m. and continued for two 45-minute periods, ending at $10^h\ 48^m$ a. m. During the whole experiment the subject lay very quietly on his back, without reading, save near the close of the first period,

when he moved considerably. After the experiment was over he seemed to be very tired and glad that it was over. Before coming to the laboratory the subject urinated at $7^h 30^m$ a. m., and again, after the experiment, at $11^h 03^m$ a. m. The records of the experiment are given in table 74.

TABLE 74.—*Measurements of metabolism—Calorimeter experiment No. T1.*

Date and period.	Carbon dioxide eliminated.		Oxygen absorbed.		Respiratory quotient.	Average pulse-rate.	Average respiration rate.
	Total.	Per minute.	Total.	Per minute.			
Feb. 14, 1911:	*gms.*	*c.c.*	*gms.*	*c.c.*			
[1] $9^h 18^m$ a.m. to $10^h 03^m$ a.m.	15.0	170	15.0	233	0.73	66	15
10 03 a.m. 10 48 a.m.	15 2	172	15 8	246	.70	66	16
Total 1 hr. 30 min.[2]	30.2	171	30.8	240	....	..	.

[1] Subject drank a cup of coffee at $6^h 30^m$ a.m.
[2] Carbon dioxide eliminated per kilogram per minute, 3.32 c.c.; oxygen absorbed per kilogram per minute, 4.66 c.c. The urine collected between $7^h 30^m$ a.m. and $11^h 03^m$ a.m. amounted to 345 c.c., specific gravity 1.030, and contained 1.52 gms. nitrogen and 12.4 gms. sugar.

CALORIMETER EXPERIMENT No. T2.

Date, February 16, 1911. Body-weight without clothing, 51.3 kilos.

This was also a fasting experiment, neither food nor coffee being taken after the evening meal of the day before. The subject came to the laboratory at $7^h 30^m$ a. m., and the experiment began at $8^h 47^m$ a. m. After two 45-minute periods the experiment ended at $10^h 17^m$ a. m. Throughout the whole experiment the subject lay quietly on his back. He appeared to be somewhat tired at the end of the experimental period, but had evidently become more accustomed to the apparatus and the routine. The pulse and respiration rates were obtained in the usual way with the stethoscope and pneumograph, a second pneumograph being used about the thighs to give a record of any major movements. The subject urinated at $7^h 42^m$ a. m., but was unable to urinate again after the experiment was over. The records of the experiment are given in table 75.

TABLE 75.—*Measurements of metabolism—Calorimeter experiment No. T2.*

Date and period.	Carbon dioxide eliminated.		Oxygen absorbed.		Respiratory quotient	Average pulse-rate.	Average respiration rate
	Total.	Per minute.	Total.	Per minute.			
Feb. 16, 1911:	*gms.*	*c.c.*	*gms.*	*c.c.*			
$8^h 47^m$ a.m. to $9^h 32^m$ a m.	14 8	168	14 0	217	0 77	67	15
9 32 a.m. 10 17 a.m.	14 7	167	14.7	229	73	69	15
Total 1 hr. 30 min.[1]	29.5	167	28 7	223	....	..	

[1] Carbon dioxide eliminated per kilogram per minute, 3.26 c.c.; oxygen absorbed per kilogram per minute, 4 35 c c. The urine collected between 7 and $7^h 42^m$ a.m. amounted to 80 c.c., specific gravity, 1.030, and contained 0 34 gms. nitrogen and 2.4 gms. sugar.

TABLE 76.—*Comparison of metabolism experiments in the bed calorimeter with Case T in experiments without food.*

Experiment No.	Date.	Weight of subject.	Length of experiment.	Per minute		Respiratory quotient.	Average pulse per minute.	Average respiration per minute.
				Carbon dioxide eliminated.	Oxygen absorbed.			
	1911.	*kilos.*	*hrs. min.*	*c.c.*	*c.c.*			
T 1	Feb. 14[1] ..	51.5	1 30	171	240	0.71	66	15 5
T 2	Feb. 16....	51.3	1 30	167	223	.75	68	15 0

[1] 2 hours and 48 minutes before the experiment began the subject drank a cup of coffee.

CASE U.

DESCRIPTION OF THE CASE.

Female; born November 16, 1873; single; teacher; onset of diabetes, April 1909; sugar found in the urine August 1, 1909; first came under our observation April 18, 1910; died in coma August 11, 1911.

Family history.—No history of diabetes in family. Father, mother, and two brothers well; one brother has arthritis deformans.

Past history.—Healthy; scarlet fever three times, measles, mumps, whooping cough. Pneumonia at 14. Catamenia normal. Overwork and worry, especially because of the brother's illness.

General history of case.—In April 1909 there were loss of weight and polydipsia. In May 1909, polyuria, furuncles, and weariness appeared. Following the discovery of sugar in the urine, thirst and nervousness nearly disappeared and the strength improved; nevertheless the patient had polyphagia. The course of the disease is shown in table 77. Notwithstanding the severity of the disease, the patient taught daily until May 1911. There was a gradual loss in strength, as well as in weight, and she died in coma August 11, 1911.

Physical examination.—Greatest weight, summer of 1908, 53.1 kilos.; April 1909, 49.9 kilos.; May 1909, 45.4 kilos.; August 1909, 41.7 kilos.; April 18, 1910, 39.7 kilos. Height, 160 cm. Pupils equal and reacted to light. Knee-jerks normal. Bilateral submaxillary glands. Emaciated. Tongue and teeth normal. Heart just within mammillary line, systolic at the apex. Pulse-rate, 112. Blood-pressure, 100. Lungs normal. Abdomen, right movable kidney but otherwise normal. No edema of lower extremities.

Urine data.—The quantity of urine August 1, 1909, was 5,750 c.c.; specific gravity 1.040. The reaction of the urine was acid throughout the period of observation. The acidosis was marked from the very first, but decreased subsequently with the use of sodium bicarbonate. The greatest quantity of ammonia was 5.2 grams, April 22, 1911. On March 11, 1911, the urinary sediment contained numerous fine and coarse granular casts. The quantity of sugar in the urine when the patient first came under observation amounted to 7.2 per cent in a single specimen, and to 6.2 per cent (132 grams) during the 24 hours of April 19–20, 1911. This steadily decreased, but the patient never became sugar-free. Albumen never exceeded a slight trace.

EXPERIMENTS WITH CASE U.

With this subject three bed calorimeter experiments were made and nine respiration experiments. A number of these were made in series. Series I included a calorimeter experiment (U 5) in which the subject fasted, and a respiration experiment (U 6). In this latter experiment the subject fasted the first two periods, then took food. Series II, which included five experiments, began with a respiration experiment (U 8), which was followed by an oatmeal breakfast; an experiment was then made with the bed calorimeter (U 9), which was in turn succeeded by a second respiration experiment (U 10). The subject spent the night in the bed calorimeter, metabolism measurements being made during the latter part of the night (U 11). In the morning of the next day, a third respiration experiment (U 12) was made after a beefsteak breakfast, completing the series. A comparison of the data obtained in the calorimeter experiments is given in table 92. The vital statistics for this subject are as follows:

Date of birth, November 16, 1873; height, 160 cm.; range of body-weight without clothing during experiments, 35.8 to 44.2 kilos.

TABLE 77.—*Clinical chart—Case U.*

Date.	Volume of urine.	Specific gravity.	Diacetic acid.	β-oxybutyric acid.	Nitrogen.	Ammonia. Total.	Ammonia. NH3-N / Total N	Sugar. By copper reduction.	Sugar. By rotation.	Diet.[1] Carbohydrate.	Diet.[1] Nitrogen.[2]	Diet.[1] Alcohol.	Carbohydrate balance.	NaHCO3.	Body-weight without clothes.
1910.	*c.c.*			*gms.*	*gms.*	*gms.*	*p. ct.*	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*kilos.*
Apr. 17–18..	....	1039	0	....	....	...	...	+	[3]7 2	...	..	...		..	....
Apr. 19–20	2125	1042	V. sl.+	....	....	...	...	+	132	...	..	..		..	....
Apr. 22–23	2000	1032	V. sl.+	....	....	...	...		68	...	..	..		..	....
Apr. 25–26	1875	1030	0	....	....	...	....	....	79	70	12	..	−10	..	39.5
Apr. 29–30.	2000	1031	++		....	..	....	+	60	80			+20	..	40.2
May 1– 2 .	2000	1030	+	....	....	..	....	....	56	70	..	12	+15	..	40.4
May 4– 5	2375	1033	+	....	....	...	....	....	67	80		15	+15	..	39.5
May 9–10 .	2190	1023	+	....	....	..	....	....	31	65	..	15	+35	..	39.0
May 13–14..	2500	1026	+	....	11.5	4 4	31.5	....	60	75		15	+15	(4)	38.3
May 18–19[5].	2125	1027	+	....	9.0	4.3	39.3	74	51	100	..	9	+25	8	39.3
May 19–20..	**[6]325**	....	......	....	**1 2**	...	....	**15**	...	...	..	..	...	..	....
May 23–24 .	2250	1034	++	....	10.7	3.5	26.9	104	86	70		..	−35	16	40.5
May 25–26 .	2000	....	......	....	9.8	...	....	77	..	95	..	..	+20	..	....
May 26–27[7]	**275**	....	......	....	**0.6**	...	....	**3**	...	...	..	..	..	..	....
June 27–28	2500	1035	++	....	25.5	...	....	[8]135	120	80	..	12	−55	16	42.3
July 8– 9 .	....	1035	......	....	....	...	....	....	...	...	..	..	...	..	....
July 14–15	2000	1034	++	....	....	1.7	....	....	64	75	15	12	+10	16	....
July 25–26..	....	1032	......	....	....	...	....	....	...	...	..	..	...	..	43.3
Aug. 1– 2	2375	1026	+++	....	13.8	...	....	50	52	75	13	12	+25	16	41.8
Aug. 17–18..	....	1030	......	....	....	..	....	....	...	...	..	..	..	..	43.6
Sept. 12–13..	2500	1029	+++	...	13.3	..	....	98	90	75	19	12	−25	12	44 0
Oct. 7– 8.	2000	1030	++++	19.7	10.0	2.8	23.0	72	52	85	12	12	+15	16	43.6
Nov. 4– 5..	2750	1028	++++	....	....	..	....	....	77	80	16	12	+ 5	16	41.1
Nov. 22–23..	2750	1033	+++	....	13 3	...	....	+	105	76	..	12	−30	16	41.1
Dec. 16–17..	2750	1031	++++	....	....	4 1	....	....	88	70±	11±	12	−20	12	40.9
1911.															
Jan. 13–14..	2750	1031	++++	....	....	4.0	...	....	99	75	.	12	−25	12	40.4
Feb. 10–11..	3250	1025	+++	....	13.4	4.4	27.0	117	91	75	12±	12	−40	12	38 2
Mar. 10–11 .	[9]3000	1024	+++	....	....	4 7	....	90	66	65	..	12	−25	16	37.2
Mar 24–25.	3250	1030	++	30.0	12.5	5.0	32 9	156	137	75	15±	12	−80	12	39.5
Mar. 31 – Apr. 1....	**2420**	....	......	**22.3**	**9.5**	**3 6**	**31 2**	**120**	...	...	..		..	..	....
Apr. 1– 2..	[10]2330	....	......	27 3	9 2	3.7	33.1	75	...	...	..		...	..	....
Apr. 2– 3	**3135**	....	......	**20.6**	**9 9**	**4 0**	**33 2**	**97**			..		...	..	....
Apr. 21–22.	3000	1029	+++	.	13 6	5 2	31.4	105	84	65	16	12	−40	12	37.7
May 19–20.	3250	1029	+++	...	....	4 7	....	127	98	55	..		−70	12	37.0
May 31 – June 1....	....	1032	......	...	[3]0.42	...	....	[3]4.74	...	...	..		.	..	....
June 1–2[11]...	....	....	......	25 5	....	..	....	....	...	...	..		.		....
June 2–3[12]..	**1805**	**1021**	......	**18.0**	**6.9**	...	....	**36**	...	...	..				....
July 6–7....	3500	1027	++	....	....	...	....	158	126	75	18±	9	−85	12	36.1

[1] Fat in diet, May 9–10, 175 gms.; Dec. 16–17, 150± gms.
[2] Approximate.
[3] Per cent.
[4] 16 gms. $NaHCO_3$ given daily, May 14, 15, and 16.
[5] 120 gms. oatmeal, 120 gms. butter, 240 c.c. cream, 240 c.c. milk, 4 eggs.
[6] From 8^h 30^m to 11^h 50^m a.m., May 19.
[7] From 7 to 9^h 45^m a.m., May 26.
[8] By fermentation.
[9] Urinary sediment contained fine and coarse granular casts.
[10] 23 hours 40 minutes.
[11] 12 hours.
[12] 23 hours 25 minutes.

RESPIRATION EXPERIMENT NO. U1.

Date, May 14, 1910. Body-weight without clothing, 39.0 kilos.

This experiment was made simply to accustom the subject to the respiration apparatus, and consisted of but one 10-minute period, beginning at 9^h 55^m a.m. The breakfast for that morning was an egg and an orange. The stethoscope and pneumograph were not used, and no records of pulse and respiration were taken other than two records of the respiration from the tension equalizer, which gave an average of 20 respirations to the minute. The carbon dioxide eliminated per minute was 155 c.c., and per kilogram per minute 3.97 c.c. The oxygen absorbed per minute was 210 c.c., and per kilogram per minute 5.38 c.c. The respiratory quotient was 0.74.

RESPIRATION EXPERIMENT No. U 2.

Date, May 19, 1910. Body-weight without clothing, 39.3 kilos.

A breakfast consisting of a dish of oatmeal, an egg, a piece of bacon, and a cup of coffee was taken before the experiment. The day preceding was an "oatmeal day," and as the subject usually felt considerably better on these days, it seemed desirable to determine the respiratory quotient under such circumstances.

The subject arrived at the laboratory about $10^h 15^m$ a.m., lay down on the couch at $10^h 30^m$ a. m., and the experiment began at $10^h 40^m$ a. m., continuing for three periods of 10 to 11 minutes, with intermissions of 9 to 12 minutes. The subject urinated before the experiment at $8^h 30^m$ a. m., and afterwards at $11^h 50^m$ a. m. The records of the experiment may be found in table 78.

TABLE 78.—*Results of respiration experiment No. U 2.*

Date and time.	Duration.	Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration rate.
May 19, 1910:	*min. sec.*	*c.c.*	*c.c.*			
$10^h 40^m$ a.m.[1]	10 31	164	222	0.74	90	17
11 01 a.m.	10 37	157	212	74	86	17
11 24 a.m.	10 05	153	217	.71	87	17
Average	....	[2]158	[2]217	73	88	17

[1]The subject had eaten breakfast as usual.

[2]Carbon dioxide eliminated per kilogram per minute, 4.02 c.c.; oxygen absorbed per kilogram per minute, 5.52 c.c. The urine collected between $8^h 30^m$ and $11^h 50^m$ a.m. amounted to 323 c.c. and contained 1.20 gms. nitrogen and 15 gms. sugar.

RESPIRATION EXPERIMENT No. U 3.

Date, May 26, 1910. Body-weight without clothing, 41.2 kilos.

The subject came to the laboratory without breakfast about $8^h 30^m$ a. m., and lay down upon the couch for 10 minutes before the experiment began at $8^h 44^m$ a. m. Three periods of about 10 minutes each were included in the experiment, with intermissions of 10 to 12 minutes. The subject urinated at 7 a. m. before coming to the laboratory, and again at $9^h 45^m$ a. m. After the experiment was over she was given a breakfast consisting of oatmeal with cream, and boiled eggs. The records of the experiment are given in table 79.

TABLE 79.—*Results of respirotion experiment No. U 3.*

Date and time.	Duration.	Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration rate.
May 26, 1910:	*min. sec.*	*c.c.*	*c.c.*			
$8^h 44^m$ a.m.	10 03	160	215	0 74	85	17
9 04 a.m.	9 58	152	182 (?)	84 (?)	89	16
9 26 a.m.	9 52	152	214	71	89	16
Average	....	[1]155	[1]204	76	88	16

[1]Carbon dioxide eliminated per kilogram per minute, 3.76 c.c.; oxygen absorbed per kilogram per minute, 4.95 c.c. The urine collected between 7 and $9^h 45^m$ a. m. amounted to 274 c.c. and contained 0.64 gm. nitrogen and 2.8 gms. sugar.

RESPIRATION EXPERIMENT No. U 4.

Date, September 13, 1910. Body-weight without clothing, 44.2 kilos.

This experiment followed a breakfast taken at $6^h 45^m$ a. m. consisting of oatmeal and cream, small amounts of melon and bacon, and an egg. She reached the laboratory at $10^h 45^m$ a. m., and almost immediately lay down

upon the couch. The experiment began at 11 a. m., continued for three periods of 12 to 13 minutes each, with intermissions of 12 to 16 minutes. Throughout the whole experiment the subject was very calm and quiet. The results of the experiment are given in table 80.

TABLE 80.—*Results of respiration experiment No. U 4.*

Date and time.	Duration.	Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration rate.
Sept. 13 1910:	*min. sec.*	*c.c.*	*c.c.*			
$11^h 00^m$ a.m.[1]..	12 14	158	224	0.71	90	18
11 28 a.m....	13 12	154	221	.70	88	18
11 53 a.m. ..	12 11	151	212	.71	90	17
Average......	....	[2] 154	[2] 219	.71	89	18

[1] Subject ate breakfast at $6^h 45^m$ a.m.
[2] Carbon dioxide eliminated per kilogram per minute, 3.48 c.c.; oxygen absorbed per kilogram per minute, 4.95 c.c.

CALORIMETER EXPERIMENT No. U 5.

Date, March 31, 1911. Body-weight without clothing, 39.9 kilos.

This was the initial experiment of Series I, and the first with this subject in the bed calorimeter. She arrived at the laboratory at $7^h 40^m$ a. m., without breakfast, and entered the apparatus at $7^h 55^m$ a. m. The experiment began at $8^h 50^m$ a. m., continuing for two 45-minute periods, ending at $10^h 20^m$ a. m. The subject lay very quietly reading during all of the experiment, except near the end of the periods. Both pneumographs and the stethoscope were used to obtain the respiration-rate, the muscular activity, and the pulse-rate. The results of the experiment are given in tables 81 and 83.

TABLE 81.—*Measurements of metabolism—Calorimeter experiment No. U 5.*

Date and period.	Carbon dioxide eliminated.		Average pulse-rate.	Average respiration rate.
	Total.	Per minute.		
Mar. 31, 1911:	*gms.*	*c.c.*		
$8^h 50^m$ a.m. to $9^h 35^m$ a.m......	13.6	154	84	18
9 35 a.m. 10 20 a.m......	13.8	157	84	19
Total 1 hr. 30 min.[1]..........	27.4	155	..	..

[1] Carbon dioxide eliminated per kilogram per minute, 3.88 c.c.

RESPIRATION EXPERIMENT No. U 6.

Date, March 31, 1911. Body-weight without clothing, 39.9 kilos.

This experiment, which was the second and last of Series I, was divided into two parts, the subject continuing to fast after leaving the bed calorimeter until after the first two periods had been concluded. She then took 100 grams levulose, 100 c.c. weak coffee, and 175 c.c. hot water. Six additional periods followed.

The experiment began at $10^h 50^m$ a. m., the two fasting periods ending at $11^h 38^m$ a.m. The food was taken at 12 o'clock, and the following six periods began at $12^h 16^m$ p.m., ending at $3^h 08^m$ p.m. Each period was about 15 minutes long, the intermissions ranging from 8 to 31 minutes. The subject was awake during the first period, and coughed once at $10^h 54^m$ a. m., also several times in the second period. There were slight movements reported in the fourth, seventh, and eighth periods. The subject urinated after the experiment at $3^h 15^m$ p. m. The results of the experiment may be found in tables 82 and 83.

TABLE 82.—*Results of respiration experiment No. U6.*

Date and time.	Duration.	Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration rate.
Mar. 31, 1911:						
Without food—	*min. sec.*	*c.c.*	*c.c.*			
$10^h 50^m$ a.m....	14 59	151	205	0 74	86	18
11 23 a.m....	15 0	145	211	69	88	17
Average..........	....	[1] 148	[1] 208	71	87	17
With food—						
$12^h 16^m$ p.m.[2]...	15 10	172	271	.63	90	19
12 44 p.m....	14 58	184	261	.70	90	19
1 30 p.m....	14 47	180	246	.73	.	19
2 05 p.m....	15 7	172	235	.73	87	18
2 28 p.m....	14 27	171	250	.68	89	20
2 53 p.m....	14 36	166	240	.69	89	19
Average..........	....	[3] 174	[3] 251	.69	89	19

[1] Carbon dioxide eliminated per kilogram per minute, without food, 3.71 c.c ; oxygen absorbed per kilogram per minute, without food, 5 21 c.c.
[2] Subject took 100 gms. levulose in 200 c c. of very weak coffee (hot) at 12 noon.
[3] Carbon dioxide eliminated per kilogram per minute, with food, 4.36 c.c.; oxygen absorbed per kilogram per minute, with food, 6.29 c.c

TABLE 83.—*Statistics of urine—Calorimeter experiment No. U5 and respiration experiment No. U6.*

Date and period.	Volume.	Specific gravity.	Total nitrogen.	Sugar.
Mar. 31, 1911:	*c.c.*		*gms.*	*gms.*
$7^h 00^m$ a.m. to $10^h 30^m$ a.m...	246	1.029	1.16	7 5
10 30 a.m. 3 15 p.m.[1]	555	1.030	1.50	24 5
Mar. 31–Apr. 1, 1911:				
$3^h 15^m$ p.m. to $7^h 00^m$ a.m.....	1620	.....	6.76	87.6

[1] Subject took 100 gms. levulose in 200 c.c. very weak hot coffee at 12 noon.

RESPIRATION EXPERIMENT No. U7.

Date, April 2, 1911. Body-weight without clothing, 39.8 kilos.

This experiment was (like U6) divided into two parts, the first three periods being fasting periods, and the last six periods following the ingestion of 518 grams of cooked oatmeal and 38 grams of butter.

On coming to the laboratory, the subject lay down on the couch at $7^h 47^m$ a. m., and the experiment began at $8^h 17^m$ a. m. In all of the three fasting periods, which were each 15 minutes in length with intermissions of 13 to 14 minutes, the subject was reported as awake and very quiet. The oatmeal was taken between $9^h 40^m$ and $9^h 55^m$ a. m., and the subject lay down on the couch again at 10 a. m. The six periods following the food began at $10^h 13^m$ a. m., with intermissions of the usual length, except between the last three periods, these being about an hour each. During the fourth, fifth, sixth, and seventh periods the subject was reported as restless, coughing and moving her hands and feet. Between the seventh and eighth periods the subject sat up in a chair and did not lie down on the couch again until about 15 minutes before the next period began. She was much quieter in the eighth period than previously, although she reached once for her handkerchief. She felt sleepy during this period, and took a 35-minute nap between the eighth and ninth periods. The results for this experiment are given in tables 84 and 85.

Respiration Experiment No. U 8.

Date, June 2, 1911. Body-weight without clothing, 37.1 kilos.

Before this experiment, which was the first of Series II, the subject took $\frac{1}{60}$ grain strychnine. She arrived at the laboratory at 7h 25m a. m., without breakfast, and lay down upon the couch at 7h 40m a. m. The experiment began at 8h 10m a. m., continuing for two periods of 15 minutes each, with an intermission of 12 minutes. The subject was quiet throughout the experiment, with the exception of a few movements of the hands during the second period. The results of the experiment may be found in tables 86 and 91.

Table 84.—*Results of respiration experiment No. U 7.*

Date and time.	Duration.	Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration rate.
Apr. 2, 1911:						
Without food—	*min. sec.*	*c.c.*	*c.c.*			
8h 17m a.m....	14 58	148	199	0 75	86	18
8 45 a.m....	15 3	151	203	74	90	18
9 14 a.m....	14 47	154	213	72	92	18
Average..........	....	[1] 151	[1] 205	74	89	18
With food—						
10h 13m a.m.[2]...	15 3	163	234	.70	100	18
10 39 a.m....	14 58	167	228	.73	99	19
11 08 a.m....	15 4	177	236	75	99	19
12 12 p.m....	14 54	170	230	74	86	19
1 28 p.m.[3]...	15 6	154	206	.75	88	19
2 37 p.m....	14 49	163	209	78	92	18
Average..........	....	[4] 166	[4] 224	.74	94	19

[1] Carbon dioxide eliminated per kilogram per minute, without food, 3.79 c.c.; oxygen absorbed per kilogram per minute, without food, 5.15 c.c.
[2] Subject ate 518.4 gms. cooked oatmeal and 38 gms. butter between 9h 40m and 9h 55m a.m.
[3] Subject slept about 35 minutes after this period and was awakened at 2h 31m p.m.
[4] Carbon dioxide eliminated per kilogram per minute, with food, 4.17 c.c ; oxygen absorbed per kilogram per minute, with food, 5.63 c.c.

Table 85.—*Statistics of urine—Respiration experiments No. U 7.*

Date and period.	Volume.	Total nitrogen.	Sugar.
Apr. 2, 1911:	*c.c.*	*gms.*	*gms.*
6h 40m a.m. to 7h 35m a.m........	100	0 42	2 2
7 35 a.m. 9 33 a.m........	216	71	3.7
9 33 a.m. 11 50 a.m.[1]......	425	88	10.2
11 50 a.m. 2 58 p.m........	475	1.09	18 1
Apr. 2-3, 1911:			
2h 58m p.m. to 6h 30m a.m........	1920	6.73	62.8

[1] Subject ate 518.4 gms. of cooked oatmeal and 38 gms. of butter between 9h 40m and 9h 55m a.m.

Table 86.—*Results of respiration experiment No. U 8.*

Date and time.	Duration.	Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration rate.
June 2, 1911:	*min. sec.*	*c.c.*	*c.c.*			
8h 10m a.m.....	14 56	145	203	0.71	75	18
8 37 a.m.....	14 47	142	202	.70	79	18
Average......	....	[1] 144	[1] 203	.71	77	18

[1] Carbon dioxide eliminated per kilogram per minute, 3.88 c.c.; oxygen absorbed per kilogram per minute, 5.47c.

Calorimeter Experiment No. U 9.

Date, June 2, 1911. Body-weight without clothing, 37.1 kilos.

This experiment immediately followed respiration experiment No. U 7, and was preceded by a breakfast of 477 grams of oatmeal and 157 grams of heavy cream. She also drank 200 c.c. of water. Before entering the bed calorimeter the subject urinated at $9^h 30^m$ a. m. The experiment began at $10^h 46^m$ a. m. and continued for four 45-minute periods, ending at $1^h 46^m$ p. m. The subject was very quiet, except for several slight movements, reading until $12^h 30^m$ p. m., when she was reported asleep by the nurse in attendance. At $1^h 16^m$ p. m. it was noted that the subject was again reading. The stethoscope and pneumograph were used in this experiment, but, owing to a loose adjustment, the records of the respiration were unsatisfactory. The pulse records were also difficult to obtain. The measurements of the oxygen indicated a leak, but it was not located. The measurements of the metabolism and other records made during the experiment are given in tables 87 and 91.

Table 87.—*Measurements of metabolism—Calorimeter experiment No. U 9.*

Date and period.	Carbon dioxide eliminated. Total.	Carbon dioxide eliminated. Per minute.	Average pulse-rate.
June 2, 1911:	*gms.*	*c.c.*	
$10^h 40^m$ a.m. to $11^h 31^m$ a.m.[1]	14.6	166	87
11 31 a.m. 12 16 p.m.	15.2	171	87
12 16 p.m. 1 01 p.m.	14.0	158	85
1 01 p.m. 1 46 p.m.	14.5	164	89
Total, 3 hours[2]	58.3	165	

[1] Subject ate 477 gms. cooked oatmeal and 157 gms. cream between $9^h 06^m$ and $9^h 25^m$ a.m.
[2] Carbon dioxide eliminated per kilogram per minute, 4.45 c.c.

Respiration Experiment No. U 10.

Date, June 2, 1911. Body-weight without clothing, 36.8 kilos.

This respiration experiment followed immediately after the experiment with the bed calorimeter (U 9) and included seven periods, each of which was approximately 15 minutes long. The intermissions ranged from 35 minutes to 1 hour and 10 minutes. The experiment began at $2^h 17^m$ p. m. and ended at $9^h 58^m$ p. m. The subject was very quiet and awake throughout the experiment. A period was begun in the intermission between the first and second periods, but as the subject moved her head and there was the possibility of a

Table 88.—*Results of respiration experiment No. U 10.*

Date and time	Duration.	Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration rate.
June 2, 1911:	*min. sec.*	*c.c.*	*c.c.*			
$2^h 17^m$ p.m.[1]	14 40	142	207	0.69	84	19
3 20 p.m.	14 42	147	204	.72	86	19
4 29 p.m.	15 2	141	202	.70	84	20
5 47 p.m.	14 31	143	202	.71	82	20
6 57 p.m.	14 35	140	203	.69	84	21
8 22 p.m.	15 2	133	200	.67	82	19
9 43 p.m.	15 2	134	196	.68	82	20
Average		[2] 140	[2] 202	.69	83	20

[1] The subject had eaten oatmeal and cream between $9^h 06^m$ a.m. and $9^h 25^m$ a.m.
[2] Carbon dioxide eliminated per kilogram per minute, 3.80 c.c.; oxygen absorbed per kilogram per minute, 5.49 c.c.

leak, the measurements were discontinued at the end of approximately 2 minutes. Between the second and third, third and fourth, and the fifth and sixth periods she sat up in a chair, lying down on the couch again 13 to 20 minutes before the beginning of the following period. The nurse gave her a massage in the intermission between the fourth and fifth periods. Previous to the experiment the subject drank 120 c.c. of water. She also urinated at 1^h 50^m p. m., and again at 5^h 10^m p. m., 6^h 40^m p. m., and 10^h 30^m p. m. The results of the experiment are given in tables 88 and 91.

Calorimeter Experiment No. U 11.

Date, June 2–3, 1911. Body-weight without clothing, 36.2 kilos.

In this experiment (the fourth of Series II) the subject remained in the bed calorimeter all night, with one short intermission. At 10 p. m. the nurse in attendance gave her an alcohol rub-down in preparation for the experiment. The subject also drank a glass of water at 10^h 50^m p. m., just before entering the apparatus, but took no food. The experiment was divided into two parts; the first part began at 11^h 55^m p. m. and continued for one period of 1 hour and 32 minutes, and a second of 1 hour and 47 minutes, ending at 2^h 14^m a. m. The subject was then taken out of the calorimeter for a short time, but returned to the apparatus at 2^h 40^m a. m., the second part of the experiment beginning at 4^h 01^m a. m. In this section of the experiment the measurements were also

Table 89.—*Measurements of metabolism—Calorimeter experiment No. U 11.*

Date and period.	Carbon dioxide eliminated.		Oxygen absorbed.		Respiratory quotient.	Average pulse-rate.
	Total.	Per minute.	Total.	Per minute.		
June 2–3, 1911:	*gms.*	*c.c.*	*gms.*	*c.c.*		
11^h 55^m p.m. to 1^h 27^m a.m.	24 4	135	23.3	177	0 76	83
1 27 a.m. 2 14 a.m.	15.2	163	....	..	.	80
4 01 a.m. 5 05 a.m.	18 3	145	....	..	.	82
5 05 a.m. 6 05 a.m.	15.1	128	15.6	183	.70	83
Total 4 hrs. 23 min.	73.0	[1] 141	38.9	[2] 179	..	

[1] Carbon dioxide eliminated per kilogram per minute, 3.90 c.c.
[2] Oxygen absorbed per kilogram per minute (2 hrs. 32 min.), 4.94 c c.

made in two periods, the first 1 hour and 4 minutes and the second 1 hour in length. No records of the body-temperature were obtained, and the pneumograph was not used, but the pulse-rate was taken by means of the stethoscope. The subject slept throughout the first period, but waked at the end, and her slight movement at this time disturbed the measurement of the oxygen. At the beginning of the next period she fell asleep again, and slept until taken out of the calorimeter. After reentering the apparatus she slept the rest of the night and was very quiet. The experiment did not appear to disturb the subject at all, for she was rested by her night's sleep and said that she had slept better than she did at home. No water was taken during the experiment. Urine was passed at 6^h 40^m and 10^h 30^m p. m. June 2, and at 2^h 25^m and 6^h 25^m a. m. June 3. The records of the experiment are given in tables 89 and 91.

Respiration Experiment No. U 12.

Date, June 3, 1911. Body-weight without clothing, 35.8 kilos.

The last experiment of Series II was preceded by a breakfast of 153 grams of beefsteak, taken at 7^h 42^m a. m. With the steak, the subject drank 150 c.c. of water. She lay down upon the couch at 8^h 15^m a. m., and the experiment began at 8^h 41^m a. m., continuing for five periods 13 to 15 minutes in length, with intermissions ranging from 17 to 45 minutes. The subject complained

that the nosepieces hurt her a little in the first period. In the second she moved rather more than usual, but was quiet in the other periods. After the third period she sat up, lying down again 20 minutes before the fourth period began. The subject urinated at 10^h 17 a. m. and 11^h 45^m a. m. The results of the experiment are given in tables 90 and 91.

TABLE 90.—*Results of respiration experiment No. U 12.*

Date and time.	Duration.	Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration rate.
June 3, 1911:	*min. sec.*	*c.c.*	*c.c.*			
8^h 41^m a.m.[1]...	14 42	140	219	0.64	88	21
9 20 a.m ..	12 41	165	240	.68	90	22
9 50 a.m...	12 54	165	236	.70	90	23
10 48 a.m....	14 35	156		..	90	21
11 26 a.m....	14 20	156	223	.70	91	21
Average ...	....	[2]156	[2]230	.68	90	22

[1] Subject ate 153 gms. of beefsteak between 7^h 30^m and 7^h 42^m a.m.
[2] Carbon dioxide eliminated per kilogram per minute, 4.36 c.c.; oxygen absorbed per kilogram per minute, 6.42 c.c.

TABLE 91.—*Statistics of urine—Calorimeter experiments Nos. U 9 to U 11, and respiration experiments Nos. U 8 to U 12.*

Date and period.	Volume.	Specific gravity.	Total nitrogen.	Sugar.
June 1-2, 1911:	*c.c.*		*gms.*	*gms.*
7^h 00^m p.m. to 7^h 00^m a.m	1680	1 027	7 37	46.5
June 2, 1911:				
7^h 00^m a m to 9^h 30^m a.m [1].	209	1 024	.94	3.9
9 30 a.m. 1 50 p.m ..	782	1.018	1 88	18.9
1 50 p m 5 10 p.m ..	295	1 023	.95	6 4
5 10 p.m. 6 40 p.m	118	1.023	.49	2 3
6 40 p.m. 10 30 p.m..	146	....	.93	1.6
June 2-3, 1911:				
10^h 30^m p.m. to 2^h 25^m a.m....	146	1 022	.96	1.2
June 3, 1911:				
2^h 25^m a.m. to 6^h 25^m a.m.....	108	1.023	68	1 4
6 25 a.m. 10 17 a.m.[2]....	305	1.024	1.99	5 3
10 17 a.m. 11 45 a.m . .	81	1.034	.82	2 3

[1] Subject ate 477 gms. of cooked oatmeal and 157 gms. of cream between 9^h 06^m and 9^h 25^m a.m.
[2] Subject ate 153 gms. beefsteak between 7^h 30^m and 7^h 42^m a.m. and drank 150 c.c. of water.

TABLE 92.—*Comparison of metabolism experiments in the bed calorimeter with Case U.*

EXPERIMENTS WITHOUT FOOD.

Experiment No.	Date.	Weight of subject.	Length of experiment.	Per minute. Carbon dioxide eliminated.	Per minute. Oxygen absorbed.	Respiratory quotient.	Average pulse per minute.	Average respiration per minute.
	1911.	*kilos.*	*hrs. min.*	*c.c.*	*c.c.*			
U 5	Mar. 31	39 9	1 30	155	...	....	84	18 5
U 11	June 2-3	36.2	4 23	141	[1]179	[1]0.73	82	....
EXPERIMENTS WITH FOOD.								
	1911.	*kilos.*	*hrs. min.*	*c.c.*	*c.c.*			
U 9	June 2[2]	37 1	3 00	165	...	....	87	....

[1] Oxygen absorbed and respiratory quotient for the time included in the periods 11^h 55^m p.m. to 1^h 27^m a. m and 5^h 05^m to 6^h 05^m a.m.
[2] About 1 hour 30 minutes before the experiment began the subject ate 477 gms. of cooked oatmeal and 157 gms. cream.

CASE V.

DESCRIPTION OF THE CASE.

Male; born January 19, 1874; married; proprietor of a grocery; onset of diabetes July 1909; sugar found in the urine October 1909; came under our observation March 7, 1910; died February 6, 1911.

Family history.—No history of diabetes in the family. Father and one child well. Wife has had two miscarriages. Mother ill, diagnosis unknown. A brother is not rugged, and one sister died of typhoid fever.

Past history.—The patient advanced slowly at school because of "neuralgia" and headaches. Measles, mumps, two attacks of diphtheria. "Inflammation of the gall-duct," accompanied with severe pain but without jaundice, occurred three or four times at about 32 years of age. At one time considerable alcoholic liquor was used.

General history of the case.—In July 1909, polyuria and polyphagia were manifest, but polydipsia did not occur until October 1909, when sugar was found. The greatest quantity of urine reported was 4,000 c.c. in October 1909. Weakness, vertigo, palpitation, failing eyesight, insomnia, and indigestion were the chief symptoms. On March 8 to 9, 1910, the quantity of sugar amounted to 115 grams in 24 hours. With a fairly rigid diet the patient did not become sugar-free, and, indeed, bore the restriction of diet very poorly. Pneumonia is said to have developed upon February 3, 1911; the patient failed rapidly and death occurred February 6, 1911.

Physical examination.—Greatest weight without clothing, 63.5 kilos. Weight without clothing March 7, 1910, 58.3 kilos. Height 173 cm. Tour de taille 72.5 cm. Pupils equal and reacted to light. Knee-jerks normal. No edema of the extremities. Tongue and teeth normal. No cervical, right axillary, or inguinal gland. A left axillary gland. Pulse-rate 76, regular. Blood-pressure 100. Heart and lungs not abnormal. Abdomen, nothing abnormal felt.

Urine data.—The urinary record is given in table 93. Throughout the observations the urine was acid in reaction. No albumen was present, except on March 27 and 28, when there was a very slight trace. Diacetic acid was also absent, except on March 8–9, and a very slight trace on March 28.

TABLE 93.—*Clinical chart—Case V.*

Date.	Volume of urine.	Specific gravity.	Nitrogen.	Sugar. By copper reduction.	Sugar. By rotation.	Carbohydrate in diet.[1]	$NaHCO_3$	Body-weight without clothing.
1910.	*c.c.*		*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*kilos.*
Mar. 8–9	2300	1034	....	+	115	115	0	58.8
10–11	2040	1034	....	+	82	...	5	59.1
13–14	1920	1031	....	+	73	115	2	58.5
15–16	2400	1028	[1]19.3	+	72	90	.	....
18–19	1680	1014	....	+	7	50	3	58.9
21–22	1710	....	[2]14.5	41	...	.		....
22–23[2]	586	....	3.7	13	...	..	..	....
25–26	2400	1023	....	..	43	50	4	58.9
27[3]	750	1021	....	+	3	...		....
28[3]	720	1025	. .	+	3	.		. .
28[3]	1800	1018	.. .	..	32	. .		. . .
29[3]	1350	1016	.. .	..	8	. .	..	. . .
30[3]	1920	1023	.	.	46	. .		..
31[3]	900	1025	.. .	..	16	.		..

[1]Amounts only approximate [2]From 6 to $11^h\ 15^m$ a.m., Mar. 22. [3]12-hour record.

EXPERIMENTS WITH CASE V.

Only one experiment was made with this subject, the respiration apparatus being used. The vital statistics were as follows:

Date of birth, January 19, 1874; height, 173 cm.; body-weight, without clothing, during experiments, 60 kilos.

RESPIRATION EXPERIMENT NO. V 1.

Date, March 22, 1910. Body-weight without clothing, 60 kilos.

The subject had inadvertently eaten some breakfast at 6^h 45^m a. m. on the day of the experiment, consisting of a 2-egg omelet and a cupful of coffee. He arrived at the laboratory at 8^h 40^m a. m., lay down on the couch at 8^h 45^m a. m., and the experiment began at 9^h 22^m a. m., continuing for five periods, with the usual intermissions. Two pneumographs were used to obtain the respiration rate and the major muscular movements, and the stethoscope was employed for securing the pulse-rate. The mouth was covered with surgeon's plaster in all the periods. Just before the close of the third period the subject almost went to sleep. After the experiment he said that he found it more difficult to breathe through the apparatus than into the open air. Before coming to the laboratory in the morning he urinated at 6 a. m., after reaching the laboratory at 8^h 45^m a. m., and again after the experiment at 11^h 15^m a. m. The records of the experiment may be found in tables 94 and 95.

TABLE 94.—*Results of respiration experiment No. V 1.*

Date and time.	Duration.	Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration rate.
Mar 22, 1910:	*min. sec.*	*c.c.*	*c.c.*			
9^h 22^m a.m.[1]...	10 07	222	285	0.78	69	11
9 40 a.m....	14 50	204	291	.70	68	12
10 02 a.m....	14 36	198	283	.70	66	15
10 27 a.m....	14 19	204	274	.75	66	13
10 56 a.m....	14 24	195	280	.70	66	15
Average.....	....	[2] 205	[2] 283	.73	67	13

[1] Subject ate a light breakfast consisting of a 2-egg omelet and a cup of coffee at 6^h 45^m a.m.
[2] Carbon dioxide eliminated per kilogram per minute, 3.42 c.c.; oxygen absorbed per kilogram per minute, 4.72 c.c.

TABLE 95.—*Statistics of urine—Respiration experiment No. V 1.*

Date and period.	Volume.	Total nitrogen.	Sugar.
Mar. 22, 1910:	*c.c.*	*gms.*	*gms.*
[1] 6^h 00^m a.m. to 8^h 45^m a.m........	151	1.16	4.3
8 45 a.m. 11 15 a.m........	435	2.57	8.7

[1] Subject ate a light breakfast consisting of a 2-egg omelet and a cup of coffee at 6^h 45^m a.m.

CASE W.

DESCRIPTION OF THE CASE.

Female; born June 1, 1892; single; onset of diabetes, November 1908; sugar found in the urine January 1909; came under our observation April 30, 1910; condition November 11, 1912, comfortable.

Family history.—No history of diabetes in the family. Father had rheumatism. Mother, three brothers, and five sisters are well. Two brothers died of cholera infantum; one sister of spinal meningitis.

Past history.—Measles, mumps, chicken-pox. March 1907, operation for appendicitis, with good recovery.

General history of the case.—In November 1908 the patient was markedly tired, and in January 1909 pruritus appeared and sugar was found in the urine. In February 1909 she suffered from periods of weakness, but was not unconscious. Micturition was painful. Polyuria and polydipsia were present, but not polyphagia. During the summer of 1909 she suffered pain in the left iliac fossa, which was constant in character and accompanied by abdominal tenderness, but no fever. The pain was worse before catamenia, which was reported as normal in April 1910. Although suffering from indigestion, she vomited but once. She was nervous, and complained of dizziness, dyspnea, and palpitation. August 1909 an obstruction was found in the ureter by Dr. Chute. April 16, 1912, the patient was in comfortable health.

TABLE 96.—*Clinical chart—Case W.*

Date.	Volume of urine.	Specific gravity.	Nitrogen.	Sugar. By copper reduction.	Sugar. By rotation.	Carbohydrate in diet.[1]	Carbohydrate balance.	Body-weight without clothing.
1910.	*c.c.*		*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*kilos.*
Apr. 29–30	2000	1038	...	..	104	...	...	....
May 9–10	....	1023	...	..	[2]0.6	..	...	60 6
May 10–11	1170	1026	...	..	26	170	+145	60 7
May 11–12	1305	1021	...	..	23	170	+145	59 7
May 12–13 [3]	1980	1017	8 4	33	28	130	+ 95	60.1
May 13–14 [4]	**1575**	....	...	..	...	**130**	...	**59 1**
May 14–15 [4]	....	....	...	..	...	125	...	58.2
May 15–16 [4]	....	....	...	..	...	125	...	58 5
May 16–17	1440	1017	...	..	14	125	+110	58.5
May 17–18	1140	1021	8.8	23	16	125	+100	58 6
May 18–19	1020+	1018	...	..	[2]0.8	90	...	58.8
May 19–20	1140	1015	8.0	7	2	60	+ 55	58.9
May 20–21	1230	1015	...	tr.	1	60	+ 60	59 0
May 21–22	1740	1010	8.1	1	...	60	+ 60	58 6
May 22–23	1440	1014	8.8	1	...	60	+ 60	58 5
May 23–24	1350	1014	9.1	2	...	65	+ 65	58 9
May 24–25	**600+**	**1015**	...	0	...	...	...	**58.7**
June 1– 2	2100	1035	...	..	[5]2	...	...	...
July 5– 6	....	1023	...	0	...	...	...	....
1911.								
Aug. 9–10	...	1039	...	+	[2]6.8	...	...	....

[1] No sodium bicarbonate given except 8 gms. on May 23–24. [2] Per cent.

[3] Ammonia, 1.2 gms.; $\frac{NH_3-N}{\text{Total N}}$ = 11.8 per cent. [4] Catamenia. [5] Per cent by fermentation.

Physical examination.—Greatest weight without clothing, 63.5 kilos.; August 1909, 51.7 kilos.; April 30, 1910, 61.1 kilos. Height, 161 cm. Red cheeks. Pupils equal and reacted to light. Knee-jerks normal. No cervical, axillary, or inguinal glands felt. Pulse-rate, 112 to 128. Blood-pressure, 130. Heart 13 cm. to the left of the median line. No murmurs. Lungs normal. Liver extended 2 fingers' breadth below the costal margin. Spleen and kidney not felt. No abdominal tenderness. Scar in appendix area.

Urine data.—The greatest quantity of urine recorded was in July 1909 *i. e.*, 4500 c.c. The urinary record during observation is given in table 96. Throughout this period the reaction was acid, with an occasional slight trace of albumen. Diacetic acid was not present. The sugar in the urine decreased rapidly with moderate restriction of the diet, and disappeared within three weeks. A subsequent report, however, showed a return of sugar a few months later. Sodium bicarbonate was given only once—8 grams on May 23–24, 1910.

EXPERIMENTS WITH CASE W.

Two respiration experiments were made with this subject, in both of which she fasted. The vital statistics were as follows:

Date of birth, June 1, 1892; height, 161 cm.; range of body-weight without clothing during experiments, 58.9 to 60.1 kilos.

RESPIRATION EXPERIMENT No. W 1.

Date, May 13, 1910. Body-weight without clothing, 60.1 kilos.

The subject came to the laboratory fasting at $7^h\ 45^m$ a. m., and lay down upon the couch at $7^h\ 55^m$ a. m. The experiment began at $8^h\ 07^m$ a. m., continuing for four periods of 10 to 11 minutes each, with intermissions of 10 to 14 minutes. The subject was nervous throughout the whole experiment, especially in the last period; the respiration was consequently irregular. At the close of the second period she said that her nose felt as if it were bleeding. Just after the beginning of the third period she opened her mouth. After the experiment was over the subject felt a little faint. She seemed to breathe easily through the nose, and but for the nervousness was a very good subject. The records of the experiment are given in table 97.

TABLE 97.—*Results of respiration experiment No. W 1.*

Date and time.	Duration.	Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration rate.
May 13, 1910:	*min. sec.*	*c.c.*	*c.c.*			
$8^h\ 07^m$ a.m.	10 24	171	238	0.72	110	18
8 28 a.m.	10 39	170	228	.75	100	16
8 53 a.m.	10 17	161	...	..	106	16
9 13 a.m.	10 27	165	239	.69	100	16
Average	....	[1]167	[1]235	.72	104	17

[1] Carbon dioxide eliminated per kilogram per minute, 2.78 c.c.; oxygen absorbed per kilogram per minute, 3.91 c.c. The urine collected between 7 and $10^h\ 10^m$ a.m. amounted to 197 c.c. and contained 0.94 gm. nitrogen and 1.6 gms. sugar.

RESPIRATION EXPERIMENT No. W 2.

Date, May 24, 1910. Body-weight without clothing, 58.9 kilos.

This was also a fasting experiment, the subject having taken no food since the evening meal of the day before. She arrived at the laboratory at $8^h\ 15^m$ a. m., lay down on the couch at $8^h\ 30^m$ a. m., and the experiment began at $8^h\ 43^m$ a. m., continuing for three 10-minute periods, with intermissions of 11 to 14 minutes. She was not nearly so nervous as in the previous experiment, but as the periods continued became more restless, and at the close of the last period felt faint. The results of the experiment are given in table 98.

TABLE 98.—*Results of respiration experiment No. W 2.*

Date and time.	Duration.	Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration rate.
May 24, 1910:	*min. sec.*	*c.c.*	*c.c.*			
$8^h\ 43^m$ a.m.	10 0	157	207	0.76	91	16
9 07 a.m.	9 40	160	219	.73	91	16
9 28 a.m.	9 53	164	...	..	99	16
Average	....	[1]160	[1]213	.75	94	16

[1] Carbon dioxide eliminated per kilogram per minute, 2.72 c.c.; oxygen absorbed per kilogram per minute, 3.62 c.c. The urine collected between 7 and $9^h\ 45^m$ a.m. amounted to 162 c.c. and contained 0.57 gm. nitrogen and 0.1 gm. sugar.

CASE X.

DESCRIPTION OF THE CASE.

Male; born October 1875; married; clerk in grocery store; onset of diabetes, July 1908; sugar found in urine September 1908; came under our observation, February 28, 1910; condition, May 8, 1912, comfortable.

Family history.—No history of diabetes in the family. Father, mother, three brothers, four sisters, and one child well. A brother and a sister died soon after birth.

Past history.—Measles, mumps, whooping-cough, jaundice at 8 or 10 years of age. Twelve years and three years previous to observation, there was a swelling in the right knee for periods of 6 weeks and 10 days, respectively.

TABLE 99.—*Clinical chart—Case X.*

Date.	Volume of urine.	Specific gravity.	Diacetic acid.	Nitrogen.	Sugar. By copper reduction.	Sugar. By rotation.	Diet.[1] Carbohydrate.	Diet.[1] Nitrogen.	Diet.[1] Alcohol.	Carbohydrate balance.	Body-weight without clothing.
1910.	*c.c.*			*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*gms.*	*kilos.*
Feb. 27-28 [2]	2850	1039	0	25.9	209	194	...	..	..	..	62.3
Feb. 28-Mar. 1 [3] ..	2625	1041	0	23 8	182	179	...	..	..	.	62.3
Mar. 1- 2.......	1740	1042	0	20.7	109	101	115	..	..	+ 5	62.7
Mar. 2- 3.......	2070	1040	0	22.9	124	116	115		..	−10	63.1
Mar. 3- 4.......	2565	1038	0	....	...	133	115	..	..	−20	62.3
Mar. 4- 5.......	1890	1033	0	....	...	49	15	..	..	−35	63 0
Mar. 5- 6.......	2115	1029	0	....	...	72	75		..	+ 5	62 8
Mar. 6- 7.......	1650	1030	0	....	...	36	50	..	..	+15	63 1
Mar. 7- 8.......	1455	1031	Sl.+	....	...	38	50	..	..	+10	63.2
Mar. 8- 9.......	1530	1027	Sl.+	....	...	28	35	..	..	+ 5	63 6
Mar. 9-10.......	2070	1023	0	....	...	21	25	..	..	+ 5	63.4
Mar. 10-11.......	1710	1023	0	....	...	17	20	12	..	+ 5	63 1
Mar. 11-12.......	1200	1026	Sl.+	11 0	...	...	15	5	18	+ 5	63.6
Mar. 12-13.......	1620	1021	0	12.9	...	...	15	8	18	+10	64 0
Mar. 13-14.......	1770	1017	0	11 3	...	0	15	8	18	+10	63.4
Mar. 14-15.......	2280	1020	0	12.8	...	...	15	10	18	+10	64 4
Mar. 15-16.......	2640	1025	0	12.9	...	0	15	12	18	+15	64.7
Mar. 16-17.......	2670	1019	0	19.3	.	...	15	14	18	+10	64.6
Mar. 17-18.......	**1730**	**1017**	0	**13.0**	...	...	15	..	..	+10	....
Apr. 3- 4.......	....	1029	0	....	...	[4]0.8	15	..	..	....	64.6
Apr. 10-11.......	1470	....	0	....	...	...	...	..	..	....	65.5
Apr. 14-15.......	2000	1023	0	....	+	4	15	..	..	+10	....
May 4- 5.......	1625	1028	0	....	+	([5])	...	..	..	....	....
Oct. 23-24.......	720	1028	.....	....	0	...	...	..	..	....	70 9
Dec. 1- 2.......	625	1028	Sl.+	....	0	...	20	.	..	+20	70.9
1912.											
Apr. 26-27.......	1750	1028	+	....	+	39	25	..	..	−15	70.5

[1] No sodium bicarbonate was given, except 15 gms. on Mar. 14-15 and 15-16.

[2] Ammonia, 1.9 gms.; $\frac{NH_3-N}{\text{Total N}}=6.0$ per cent. [3] Period was $22\frac{3}{4}$ hrs, *i. e.*, $8^h\ 15^m$ to 7 a.m.

[4] Per cent. [5] Less than 0.1 per cent.

The patient used considerable tobacco and ate excessively of candy and cookies, both in the grocery store and at home. Ten years previous to observation considerable alcoholic liquor was used.

General history of the case.—While the onset of the diabetes was in July 1908, the disease first attracted particular attention and was diagnosed in September 1908, because of polyuria at a horse-race. 5000 c.c. of urine were voided during the night at the onset. Other symptoms were polydipsia, polyphagia, weakness, loss of weight, a parched tongue, pain in the back, extreme constipation, impotence, and failing eyesight. Under the advice of his physician the patient ate no pork, fat, or vegetables, but drank skim milk!

The unusually favorable course of the case, despite the unpromising condition of the patient when first seen, is probably due to the change in diet, as

prior to the time of observation his diet had been unfortunate. The case illustrates the unreliability of prognosis without repeated observations upon the same patient.

Physical examination.—Greatest weight without clothing, 90.7 kilos.; July 1908, 85.3 kilos.; February 23, 1910, 64.5 kilos. Height, 170 cm. Tour de taille, 76 cm. Pupils equal and reacted to light. Knee-jerks normal. No edema of extremities. A few small left axillary glands. No acetone odor to breath. One-third of the teeth missing. Lungs and heart normal. Pulse-rate, 80. Blood-pressure, 90 (two estimations, Riva Rocci). Abdomen, nothing abnormal felt.

Urine data.—The urinary record for the period of observation is given in table 99. The reaction was acid throughout, except March 14–16, 1910, when it was alkaline. There were occasional slight traces of albumen. The quantity of sugar in the urine on February 27–28, 1910, amounted to 209 grams in 24 hours, and the ammonia to 1.9 grams. Under strict dieting, sugar disappeared from the urine after 12 days and the urine was sugar-free on December 1, 1910, the weight having risen to 71 kilos. No sodium bicarbonate was given the patient, except 15 grams on both March 14 and March 15. On April 26, 1912, the quantity of sugar reached 39 grams in 24 hours, and there was a trace of diacetic acid. The patient reported having successfully withstood an attack of pleurisy, and that the 6.8 kilos. of weight lost during that illness had been regained.

EXPERIMENTS WITH CASE X.

With this subject 3 calorimeter experiments were made, in all of which the chair calorimeter was used. The third experiment was preceded by a respiration experiment. No food was taken in any of the experiments, and a fast of at least 12 hours preceded them. A comparison of the results obtained in the calorimeter experiments is given in table 107. The vital statistics of the subject were as follows:

Date of birth, October 1875; height, 170 cm.; range in body-weight without clothing during the experiments, 62.3 to 64.6 kilos.

TABLE 100.—*Measurements of metabolism—Calorimeter experiment No. X1.*

Date and period.	Carbon dioxide eliminated.		Oxygen absorbed.		Respiratory quotient.	Average pulse-rate.	Average respiration rate.
	Total.	Per minute.	Total.	Per minute.			
Feb. 28, 1910:	*gms.*	*c.c.*	*gms.*	*c.c.*			
$10^h\ 10^m$ a.m. to $11^h\ 10^m$ a.m. . .	27.6	234	27.4	320	0.73	70	22
11 10 a.m. 12 10 p.m. . .	24.8	211	24.7	288	.73	68	22
12 10 p.m. 1 10 p.m. . .	25.4	215	24.9	290	.74	66	20
Total 3 hrs.[1]	77.8	220	77.0	299			

[1] Carbon dioxide eliminated per kilogram per minute, 3.53 c.c.; oxygen absorbed per kilogram per minute, 4.80 c.c.

CALORIMETER EXPERIMENT No. X1.

Date, February 28, 1910. Body-weight without clothing, 62.3 kilos.

The subject came to the laboratory without breakfast at $8^h\ 10^m$ a. m. and entered the chair calorimeter at $8^h\ 41^m$ a. m. The experiment began at $10^h\ 10^m$ a. m., and continued for three 1-hour periods, ending at $1^h\ 10^m$ p. m. Records of the pulse and respiration rates were obtained by means of the stethoscope and pneumograph, while body-temperature records were secured with

the rectal thermometer. The subject also used a clinical thermometer at 11ʰ 10ᵐ a. m., 12ʰ 10ᵐ p. m., and 1ʰ 10ᵐ p. m. In this and the succeeding experiments an attempt was made to obtain some record of the muscular activity of the subject by the use of a pneumatic cushion connected with a kymograph. Throughout the experiment there was but little muscular movement aside from the activity incidental to telephoning several times during

TABLE 101.—*Statistics of urine—Calorimeter experiment No. X 1.*

Date and period.	Volume.	Total nitrogen.	Sugar.
	c.c.	*gms.*	*gms.*
Feb. 28, 1910: $8^h\ 15^m$ a.m. to $1^h\ 20^m$ p.m.	227	3.43	8.9
Feb. 28 to Mar. 1, 1910: $1^h\ 20^m$ p.m. to 7 a.m.	2400	....	182.1

each period, and drinking 64 c.c. of water at $10^h\ 20^m$ a. m. Previous to the experiment the subject urinated and defecated at $8^h\ 15^m$ a. m., and urinated again at $1^h\ 20^m$ p. m. after the experiment was over, but was unable to urinate during the experimental period. The records of the experiment are given in tables 100 and 101.

TABLE 102.—*Measurements of metabolism—Calorimeter experiment No. X 2.*

Date and period.	Carbon dioxide eliminated.		Oxygen absorbed.		Respiratory quotient.	Average pulse-rate.	Average respiration rate.
	Total.	Per minute.	Total.	Per minute.			
Mar. 1, 1910:	*gms.*	*c.c.*	*gms.*	*c.c.*			
[1] $9^h\ 18^m$ a.m. to $10^h\ 18^m$ a.m.	24.2	205	20.3	236	0.87	67	21
10 18 a.m. 11 18 a.m.	24.5	208	23.0	268	.78	63	20
11 18 a.m. 12 18 p.m.	23.5	199	22.5	262	.76	59	21
Total 3 hrs.[2]	72.2	204	65.8	256	....	..	..

[1] Subject drank a cup of coffee about 2 hours before the experiment began.
[2] Carbon dioxide eliminated per kilogram per minute, 3.25 c.c.; oxygen absorbed per kilogram per minute, 4.08 c.c.

CALORIMETER EXPERIMENT NO. X2.

Date, March 1, 1910. Body-weight without clothing, 62.7 kilos.

With the exception of a cup of coffee, no food was taken by the subject before he came to the laboratory at $7^h\ 50^m$ a. m. At $8^h\ 08^m$ a. m., the subject entered the chair calorimeter; the experiment began at $9^h\ 18^m$ a. m., continued for three 1-hour periods, and ended at $12^h\ 18^m$ p. m. The records of the pulse and respiration rates were obtained as in the preceding experiment, but the rectal thermometer was not used, although records were taken by the subject with a clinical thermometer at $9^h\ 28^m$ a. m., $10^h\ 32^m$ a. m., $11^h\ 28^m$ a. m., and

TABLE 103.—*Statistics of urine—Calorimeter experiment No. X 2.*

Date and period.	Volume.	Total nitrogen.	Sugar.
Mar. 1, 1910:	*c.c.*	*gms.*	*gms.*
[1] $7^h\ 00^m$ a.m. to $9^h\ 28^m$ a.m.	143	1 90	9 8
9 28 a.m. 10 32 a.m.	58	.77	3.1
10 32 a.m. 11 35 a.m.	48	.66	2 1
11 35 a.m. 12 25 p.m.	37	.56	1.3
Mar. 1-2, 1910:			
$12^h\ 25^m$ p.m. to $7^h\ 00^m$ a.m.	1455	16.78	92.9

[1] Subject drank a cup of coffee at about $7^h\ 15^m$ (?) a.m.

12h 18m p. m. Near the end of the first period the subject was asleep, waking just after the beginning of the second period. He telephoned once in each period. The subject urinated before coming to the laboratory at 7 a. m., and three times during the experiment, *i. e.*, at 9h 28m a. m., 10h 32m a. m., and 11h 35m a. m., also at 12h 25m p. m., after the experiment was over. He drank no water. The records of the experiment are given in tables 102 and 103.

Respiration Experiment No. X3.

Date, March 17, 1910. Body-weight without clothing, 64.6 kilos.

On the experimental day the subject drank a cupful of coffee before coming to the laboratory, but ate no breakfast. He reached the laboratory at 7h 40m a. m., lay down on the couch at 7h 45m a. m., and the experiment began at 8h 58m a. m. The three periods ranged from 12 to 15 minutes in length, with intermissions from 8 to 10 minutes, the last period ending at 9h 56m a. m. After the experiment began the subject breathed slower and possibly deeper than he had previously. In the second period he took several very deep breaths. In this period, also, there was a slight leak in the nosepiece, and a new nosepiece was accordingly used for the next period. Immediately after the experiment was over the subject urinated at 9h 56m a. m., the last period being shortened on account of the pressure of urine. The records of the experiment are given in tables 104 and 106.

Table 104.—*Results of respiration experiment No. X3.*

Date and time.	Duration.	Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration rate.
Mar. 17, 1910:	*min sec.*	*c.c.*	*c.c.*			
[1]8h 58m a.m.	14 54	178	247	0.72	72	11
9 22 a.m.	14 42	179	245	.73	73	16
9 44 a.m.	12 23	189	243	.78	72	15
Average[2]	....	182	245	0.74	72	14

[1] Subject drank a cup of coffee about 1¾ hours before experiment began.
[2] Carbon dioxide eliminated per kilogram per minute, 2.82 c.c.; oxygen absorbed per kilogram per minute, 3.79 c.c.

Calorimeter Experiment No. X4.

Date, March 17, 1910. Body-weight without clothing, 64.6 kilos.

This experiment was preceded by a five-period respiration experiment (experiment No. X3). The subject drank a cupful of coffee on the morning of the experimental day, but aside from this took no food after the evening meal of the day before. He entered the chair calorimeter at 10h 08m a. m.; the experiment began at 10h 45m a. m., continued for three 1-hour periods, and ended at 1h 45m p. m. The rectal thermometer was not used, but the

Table 105.—*Measurements of metabolism—Calorimeter experiment No. X4.*

Date and period.	Carbon dioxide eliminated.		Oxygen absorbed.		Respiratory quotient.	Average pulse-rate.	Average respiration rate.
	Total.	Per minute.	Total.	Per minute.			
Mar. 17, 1910:	*gms.*	*c.c.*	*gms.*	*c.c.*			
10h 45m a.m. to 11h 45m a.m.	20.9	177	17.5	204	0.87	69	19
11 45 a.m. 12 45 p.m.	23.1	196	22.8	266	.74	70	20
12 45 p.m. 1 45 p.m.	22.9	194	19.9	232	.84	71	20
Total 3 hrs.[1]	66.9	189	60.2	234	..	..	..

[1] Carbon dioxide eliminated per kilogram per minute, 2.93 c.c.; oxygen absorbed per kilogram per minute, 3.62 c.c.

pulse and respiration records were taken in the usual way. By means of the clinical thermometer the subject made a few records of the body temperature at 10^h 55^m a. m., 11^h 55^m a. m., 12^h 55^m p. m., and 1^h 50^m p. m. During the latter part of the second period the subject was apparently asleep, and was sound asleep near the end of the third period, but awoke before the close of the

TABLE 106.—*Statistics of urine—Respiration experiment No. X 3 and calorimeter experiment No. X 4.*

Date and period.	Volume.	Total nitrogen.	Sugar.
Mar. 17, 1910:	*c.c.*	*gms.*	*gms.*
7^h 00^m a.m. to 9^h 55^m a.m.[1]	627	1.61	0.5
9 55 a.m. 1 00 p.m.	142	1.09	.2
Mar. 17–18, 1910:			
1^h 00^m p.m. to 7^h 00^m a.m.	960	10.38	2.1

[1]Subject drank a cup of coffee at about 7^h 15^m (?) a.m.

experiment. He telephoned twice during each period. Before the experiment he urinated at 9^h 55^m a. m., but was unable to urinate again until 1 p. m. No water was taken during the experimental period. The records of the experiment are given in tables 105 and 106.

TABLE 107.—*Comparison of metabolism experiments in the chair calorimeter with Case X. Experiments without food.*

Experiment No.	Date.	Weight of subject.	Length of experiment.	Per minute. Carbon dioxide eliminated.	Per minute. Oxygen absorbed.	Respiratory quotient.	Average pulse per minute.	Average respiration per minute.
	1910.	*kilos.*	*hrs. min.*	*c.c.*	*c.c.*			
X 1	Feb. 28	62.3	3 00	220	299	0.73	68	21.5
X 2	Mar. 1[1]	62.7	3 00	204	256	.80	63	20.5
X 4	Mar. 17	64.6	3 00	189	234	.81	70	19.5

[1]About 2 hours before the experiment began the subject drank a cup of coffee.

PART III.

DISCUSSION OF RESULTS AND GENERAL CONCLUSIONS.

While in general the order and method of discussion of the subjects in this publication follow that in the earlier report, as experimental evidence accumulated certain topics which were much more completely studied warranted more extensive consideration. Furthermore, while in the earlier publication it was important to emphasize more especially the relationship between the respiratory exchange and the character of the metabolism, particularly with normal individuals, here it is necessary to pay but little attention to normal metabolism, because it is believed that this phase of the study was amply treated in the earlier report. None of the experiments with food are discussed in this report pending further investigation, but the statistics for these experiments have been presented in order to record the data permanently for subsequent use.

PULSE-RATE.

In the earlier series of experiments a cursory examination of the pulse-rate taken from time to time indicated that there was apparently no marked difference between the pulse-rate of normal individuals and that of diabetics, the fluctuations in the pulse-rate of the diabetic subjects being within normal limits. It would appear from the lack of data upon the subject in the text-books of medicine and in the monographs upon diabetes mellitus that this coincides with the opinion of most clinicians, but such a conclusion rests upon negative evidence alone, since usually little attention is paid to the pulse-rate in chronic afebrile diseases of a non-circulatory type. It is quite possible that a closer study of this factor may supply much information of value.

In physiological experimentation it is frequently difficult to distinguish between the normal and the abnormal. The popular conception of a normal pulse-rate is the observation usually made by a physician in his office, which may often be affected by the muscular exercise of the patient in walking to the office, or the excitement incidental to consulting a physician. To obtain a true normal value, however, the observation should be made under conditions which would insure its being unaffected by food, exercise, or mental stimulus of any kind. Such conditions are obtained when the record is taken with the subjects lying quietly in bed without food. It seemed therefore desirable in the later researches to make a more detailed record of these values, and study carefully not only the pulse-rate of the diabetic subjects, but also of the normal subjects used for comparison. An abstract of the results is presented in tables 108 and 109, in which are given the minimum and maximum pulse-rates recorded while the subjects lay quietly without food in the bed calorimeter or on a couch in respiration experiments. The values given for the diabetics include those obtained for all of the subjects in both the earlier and the later experiments, with the exception of E and F, no records of pulse-rate being available which were taken while these subjects were lying down.

The average for all of the diabetic subjects shows a minimum pulse-rate of 65 beats per minute, and a maximum of 81 beats. The average maximum and minimum pulse-rates for the normal subjects are 54 and 74 respectively, both materially lower than the averages found for the diabetic subjects. In preparing these tables, care was taken not to include any records obviously affected by excitement or other untoward incident in connection with the experiment, three records approximately constant usually being taken as indicating the maximum or minimum. The values given can therefore be considered as representing the average normal variations in pulse-rate to be expected for normal individuals under the conditions of experimenting as employed in this laboratory, and for patients with severe diabetes. It will be seen, therefore, that both the minimum and maximum pulse-rates of normal individuals are markedly lower than those of diabetics.

TABLE 108.—*Pulse-rate of diabetic subjects.*

Subject.	Minimum.	Maximum.	Subject.	Minimum.	Maximum.	Subject.	Minimum.	Maximum.
A..........	65	86	K........	73	83	S............	57	60
B..........	56	72	L........	54	73	T..........	63	71
C..........	50	84	M........	64	80	U..........	72	97
D..........	52	58	N........	53	84	V........	62	69
G..........	69	74	O........	57	69	W........	90	111
H..........	64	90	P........	64	82	X........	72	75
I..........	117	122	Q........	61	83			
J..........	60	84	R..........	64	73	Average .	65	81

It must furthermore be remembered that in practically every instance the normal individual led a much more active life, had much greater muscular tone, and was more restless than were the diabetics. This makes the difference in pulse-rate all the more striking, since one would ordinarily expect a somewhat higher value with the more active and restless normal subjects than with the weak, sick diabetics, disinclined to any extraneous muscular motion. An examination of tables 108 and 109 shows no regularity in either the minimum or maximum pulse-rates when individual diabetics are compared with normal individuals, since some of the diabetic subjects show a minimum pulse-rate considerably lower than the average minimum pulse-rate of the normal subjects; and similarly, the normal individuals in some instances show a pulse-rate considerably higher than the average maximum pulse-rates of the diabetics. On the whole, however, a distinct tendency toward an increased pulse-rate in diabetics is here clearly shown. This increase is fully in conformity with the

TABLE 109.—*Pulse-rate of normal subjects.*

Subject.	Min.	Max.	Subject.	Min.	Max.	Subject.	Min.	Max.
A. F. G	59	62	C. H. H........	63	69	Prof. C............	48	68
T. M. C...........	56	82	M. A. M........	49	82	Miss L............	54	79
Miss J.............	66	73	Miss B	70	82	V. G..............	48	80
Miss A.............	61	75	Dr. S..........	50	61	M. B..............	50	68
Miss E. W..........	74	90	H. F. T..........	37	64	H. B. L............	55	74
Mrs. S C..........	58	70	E. P. C..........	45	59	Miss B. W.........	74	97
H. H. A.	54	96	K. H. A	40	62	D. M..............	48	72
S A. R..........	46	76	J. R............	52	74			
Dr. P. R..........	53	66	O. F. M..........	49	66	Total average..	54	74

increased metabolism previously noted and further substantiated by the evidence set forth in this report. Yet in this discussion of the pulse-rate it should be stated that it is questionable whether sufficient information with regard to normal pulse-rate has accumulated to indicate that a variation above normal of 15 per cent could be recognized. While the metabolism may be 15 per cent above normal and be accurately measured, since normal metabolism is fairly well established, a 15 per cent increase in pulse-rate could not be so easily identified. The intimate relationship between pulse-rate and metabolism is increasingly evident in practically every new publication on metabolism and shows that to-day the pulse-rate is taking on a new significance; it is not at all impossible that the degree of acidosis and the degree of metabolism may be at least approximately estimated in diabetics by a careful examination of the pulse-rate. In this connection, a reference to the later discussion on the relationship between acidosis and metabolism will be of interest. (See page 123.)

While an increased pulse-rate is invariably accompanied by an increased metabolism, it is by no means to be inferred that the increased metabolism is due exclusively to the work of the heart. In fact, from what is known of the work of the heart, it can be seen that probably but a very small proportion of the total increase can be properly ascribed to the actual muscular action of the heart itself, but that the increased pulse-rate is an excellent index of general tonus is highly probable. Unquestionably, during increased metabolism and increased pulse-rate, there is some tendency toward an increased respiration rate, but here again it is highly improbable that the muscular action involved in raising the chest-wall can in any considerable proportion account for the total increase in metabolism. On the other hand, both the increased muscular activity of the heart and the increased work of the respiratory muscles unquestionably contribute some small quota to the total increase in metabolism. We commend to the attention of the physician the importance of the pulse-rate in diabetes and particularly the value of changes in the pulse-rate in the same patient during the progress of the disease. We likewise commend to all experimenters the practice first established by Prout[1] of reporting the pulse-rate with the chemical data of each experiment.

BODY-TEMPERATURE.

In a research of this kind, measurements of body-temperature have two purposes. First, to learn whether the temperature measurements are within normal limits and, second, for use in computing the heat production. The variations in body-temperature necessitate proper corrections for heat stored when the body-temperature rises, or for heat given off, and thus not produced, as the body-temperature falls. An ideal experiment, therefore, would call for continuous measurements of body-temperature, particularly at the beginning and end of each experimental period. In this laboratory and in the laboratory of Wesleyan University, Middletown, Connecticut, much attention has been paid in the last ten years to such measurements. To obtain the most accurate

[1] Prout, Ann. Philos., 1813, 2, p. 328.

calorimetric measurements, an electrical resistance thermometer which can be inserted deep in the rectum has been used for measuring rectal temperatures, but a number of the diabetic subjects found this somewhat objectionable, although in no sense painful. Accordingly, in many instances we were obliged to content ourselves with temperatures taken in the mouth by means of a mercurial clinical thermometer of good grade. With a number of subjects, however, we were able to determine the rectal temperature by the electrical resistance method. In general, the fluctuations and actual temperature measurements ranged well within what are commonly supposed to be normal limits; only one of the diabetic subjects showed a body-temperature that could be considered in any sense above normal, and even normal individuals have indicated equally as high a temperature as did this diabetic subject.

TABLE 110.—*Body-temperature of diabetic subjects.*

Subject.	Sublingual.[1]		Rectal.[2]	
	Maximum.[3]	Minimum.[3]	Maximum.	Minimum.
	°F.	*°F.*	*°C.*	*°C.*
A	98.4 (36.90)	97.2 (36.20)	37.07	36.30
B	98.0 (36.65)	97.6 (36.45)	.....	.....
C	.....	.....	37.32	36.49
E	99.0 (37.20)	98.0 (36.65)	.....	.....
F	98.95 (37.20)	97.95 (36.65)	.....	.....
G	.....	.....	38.05	37.70
H	98.6 (37.00)	97.6 (36.45)	.....	.....
I	98.65 (37.05)	97.75 (36.55)[4]	.....	.....
J	98.55 (36.95)	98.25 (36.80)	.....	.....
K	.....	.....	37.14	36.93
L	98.3 (36.85)	97.90 (36.60)	37.71	36.56
M	.....	.....	37.11	36.44
N	98.7 (37.05)	97.02 (36.10)	.....	.....
U	98.6 (37.00)	98.4 (36.90)	.....	.....
X	98.2 (36.80)	97.1 (36.15)	.....	.....

[1] Records taken with a clinical thermometer.
[2] Records taken with an electrical resistance thermometer.
[3] Centigrade equivalents given in parentheses.
[4] For Case I there was also 97.3° F. (36.28° C.) on Feb. 23, 1911, sitting in chair after the experiment.

To give an indication of the minimum and maximum temperatures observed with the diabetics, we have collected in table 110 the values for both the sublingual temperatures taken with a mercurial thermometer and likewise the rectal temperatures taken with the electrical resistance thermometer. An inspection of the data shows that the sublingual temperatures are practically those ordinarily experienced with normal individuals in health. The rectal temperatures are almost invariably somewhat higher than are the sublingual temperatures, as would be expected from the well-known fact that temperatures in the rectum are considerably higher than those in the mouth. With one subject, Case G, the temperature was somewhat higher than normal, averaging close to 38° C. throughout the whole experiment.

Since the publication of our first report on metabolism in diabetes, a research has been concluded in this laboratory,[1] demonstrating what has hitherto been assumed, namely, that fluctuations in temperature taken deep

[1]Benedict and Slack, A comparative study of temperature fluctuations in different parts of the human body, Carnegie Institution of Washington Publication No. 155, 1911.

in the rectum are accompanied by similar fluctuations in different parts of the body. For purposes of computing the heat production, it is most necessary to know if an alteration in temperature of 0.1 degree in any one part of the body shows a like alteration in the temperature of the body as a whole, the absolute temperatures not being so significant. The investigation referred to has shown that when the rectal temperature falls 0.1 degree, there is a corresponding fall in all other parts of the body; hence it is logical to assume that a change of temperature measured in the rectum may be ascribed to that of the whole body. In computing the heat production, therefore, correction can be made for the heat lost from the body when there is a lowering in the temperature by multiplying the specific heat of the body by its weight and by the loss in temperature as measured in the rectum.

The importance, therefore, of this table is that it establishes the fact that the temperatures of diabetics as a rule range well within what are commonly supposed to be the normal limits. We wish, however, to point out here the difficulties experienced by Benedict and Slack in securing adequate and proper records of the body-temperature by means of the mercurial thermometer in the mouth. As a means of indicating the presence or absence of a high fever this method is certainly rational, but for all physiological purposes and especially for the measurement of small differences in temperature, observations taken in the mouth are wholly unsatisfactory and no reliance should be placed upon them. On the other hand, rectal temperatures should be taken deep in the rectum, the thermometer being inserted at least 5 cm. if the true internal temperature of the body is to be recorded.

BODY-WEIGHT.

Perhaps no one gross observation made during the course of diabetes mellitus is of greater significance and causes greater alarm, both to patient and physician, than the persistent loss in body-weight. On the other hand, slight changes in body-weight which may accompany dietetic alterations or the ingestion of sodium bicarbonate are looked upon as material gains and of diagnostic value, and are thus liable to be misunderstood by the patient. To interpret intelligently these changes it is necessary both for the physician and for the patient to realize the factors affecting the body-weight of normal as well as pathological cases.

Few realize that the normal individual is continually undergoing changes in body-weight throughout the 24 hours. The extent and rapidity of these fluctuations may best be shown by means of a chart obtained from observations made every hour for 24 hours. (See fig. 1.) The subject was weighed on a sensitive platform balance; the total weight of food eaten at different times was recorded, also the total weight of drinking-water when it was taken, and the weight of urine and the weight of feces when passed. In addition to being weighed every hour, the subject was weighed immediately before and after eating or drinking, passing urine, or defecating. Two series of observations were made, the results of which are shown in curves I and II. Curve I gives

a record of hourly weighings taken when the subject was awake the whole 24 hours; curve II shows the results of hourly weighings made during the waking hours, also a record of the total loss during the night sleep.

In curve I it can be seen that except at the times when food was taken there was a downward tendency of the curve throughout the whole 24 hours. As a matter of fact, the general angle of the curve with the base-line is essentially the same throughout the whole day. During this experiment the subject was engaged in experimental work in the laboratory which necessitated continous observation during the 24 hours, and hence we find no variations in the rapidity of the combustion of materials during the day or during the night. On the other hand, when the same subject spent a normal amount of time in bed asleep, the course of the curve (curve II) is somewhat different. During the day its course is essentially the same as that of curve I, but during the night

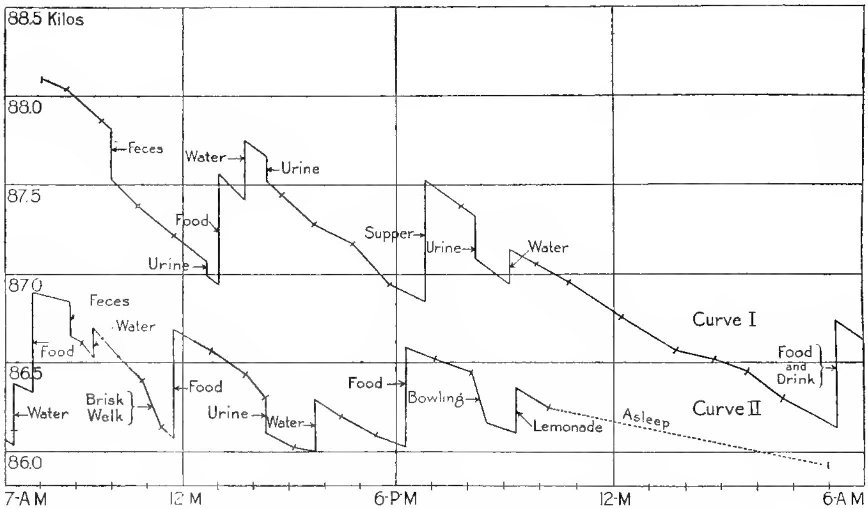

FIG. 1.—Curves showing hourly changes in body-weight for 24 hours.

Curve I shows the changes in body-weight when the subject was awake the entire 24 hours.
Curve II shows the changes in body-weight when the subject was awake from 7 a.m. to 10 p.m., and asleep from 10 p.m. to 6 a.m.

the loss is much less; this would be expected from the fact that instead of being engaged in rather active muscular work about the laboratory, the subject was in bed asleep. Curve I furthermore shows that the long night work was rather severe and the body-weight was noticeably less at the end than it was at the beginning of the experiment. In curve II the body-weight returned to essentially the same point at the end of the 24 hours, notwithstanding the fluctuations due to the ingestion of food and drink and the loss in feces and urine. The second curve shows clearly, therefore, that the body-weight varies at different times of the day, but it may be noticeably different on different days, easily varying 1 or 2 pounds in the course of a single day.

It is obvious that, aside from the loss in weight due to the passing of urine or feces, there is a general tendency for the body to lose weight from hour to

hour. This is due to a loss which has been known since the days of Sanctorius[1] as insensible perspiration. One of the best methods of observing this loss in weight in the form of insensible perspiration is during the night. If, for example, the subject is weighed just before going to bed and again in the morning immediately on rising and before the bladder is emptied, the loss in weight will be due to insensible perspiration. Two such experiments were made with a normal man weighing approximately 85 kilos. without clothing and a normal woman weighing 65 kilos. without clothing. The results are shown in table 111, which gives the number of hours spent in bed and the loss in weight in grams. The loss in weight was found to be directly proportional to the restlessness of the sleep, as on a hot, uncomfortable night it was much greater than on a cold night when the person slept quietly beneath bedclothes, instinctively moving no more than was necessary. On the average the man lost 39 grams per hour and the woman 29 grams. The insensible perspiration, therefore, was not far from 30 to 40 grams.

TABLE 111.—*Loss in body-weight during night.*

Man, 85 kilos.				Woman, 65 kilos.			
Date.	In bed.		Loss in weight.	Date.	In bed.		Loss in weight.
1898.	*hrs.*	*min.*	*gms.*	1898.	*hrs.*	*min.*	*gms.*
Oct 7....	8	45	330	Oct 13....	8	0	170
Oct. 8....	8	0	360	Oct. 14....	9	45	270
Oct 9....	8	15	300	Oct. 31....	7	15	230
Oct. 10....	9	0	310	Nov. 1....	9	0	290
Oct 11....	9	0	390				
Oct. 12....	8	15	360				
Oct. 13....	8	0	250				

Average loss per hour: Man, 39 grams: woman, 29 grams.

This observation, made with a platform balance, of the loss of 30 to 40 grams of weight by insensible perspiration received substantiation from the results of 50 or more experiments carried out in the Nutrition Laboratory by more refined and exact methods. With a considerable number of individual subjects it was found that the loss due to insensible perspiration, during waking hours, when the subject was sitting still[2] inside the respiration chamber, averaged 40 grams per hour. In certain work experiments this insensible perspiration was greatly increased, but it is safe to say that a normal person, sitting still and reading quietly, will lose in weight approximately 40 grams per hour. With severe muscular work the loss may be increased tenfold, or, indeed, during the time of strenuous muscular exercise, as in athletic contests, even a hundredfold. Although the amount of this insensible perspiration can be obtained by accurately weighing the subject on scales, the character of the loss can be determined only by careful respiration experiments, which show that carbon dioxide and water-vapor are continually being given off from the

[1] Sanctorius, De medicina statica aphorismi, Venice, 1614. Translated by John Quincy, M. D., London, 1737.

[2] Benedict and Carpenter, Carnegie Institution of Washington Publication No. 126, 1910. p. 114.

body and oxygen consumed. The loss in insensible perspiration is, then, not simply an evaporation of water from the body, but consists, in part at least, of an actual loss of organized body-tissue that has been oxidized by the oxygen taken into the lungs and given off both as carbon dioxide and as water resulting from the oxidation of organic hydrogen.

Referring again to curves I and II in fig. 1, it will be seen that the increase in weight found after taking food was due simply to the weight of the food taken into the intestinal tract, and that the noticeable losses in weight following the passage of urine and feces were due to the loss of these materials from the body. In discussing changes in body-weight, the important point to note is whether there are additions to or losses from the total body-mass, the incidental fluctuations due to the taking on of food or the passage of urine or feces being of no great importance. If, then, during a period of one year, the body gradually increases in weight a number of pounds or loses a number of pounds, it is clear that these changes in weight can not be due to minor fluctuations in the quantity of water or food taken, of urine passed, or of feces excreted.

A factor which should be taken into consideration in interpreting changes in body-weight is the fluctuation in the water-content of the body. Under certain conditions it is possible for the body to retain considerable quantities of water and, indeed, to be deprived of considerable amounts of water that would normally be retained. Since about 60 per cent of the body is water, any change of water-content may result in material gains or losses in body-weight. A man weighing, for example, 65 kilos. may have an absolute water-content of 40 kilos., so that a relatively small change in the percentage of water in the body may produce a change in body-weight of 1 kilo.

It was observed many years ago by Bischoff and Voit,[1] in a series of experiments with animals, that when the diet was in large part carbohydrate there was a tendency for the body to retain water in that the muscular tissues became more moist. By means of the respiration calorimeter at Wesleyan University, Middletown, Connecticut, an interesting experiment was made on a man which showed conclusively the effect of the constituents of a diet on the water-content of the body.[2] During the experiment, which lasted 6 days, the subject was confined inside of a respiration chamber and spent 8 hours of the day riding a stationary bicycle ergometer, thereby doing a considerable amount of muscular work. The daily routine and the quantity of work performed were adjusted so that they would be the same on all days. During the first three days the subject was given a diet containing a large amount of carbohydrate, the total diet being nearly, although not quite, sufficient to supply him with energy for the amount of work he was to do. In this period, which was preceded by a preliminary period with the same diet, the body retained its weight for a number of days. On the fourth day the character of the diet was materially altered by decreasing the carbohydrate and increasing the fat. Singularly enough, although the actual total weight of food ingested was somewhat more

[1]Bischoff und Voit, Die Gesetze der Ernährung des Fleischfressers, Leipsic, 1860.
[2]Benedict and Milner, U. S. Dept. Agr., Office Exp. Stas. Bul. 175, 1907, p. 225.

than on the first three days, nevertheless the body actually lost in weight 950, 839, and 952 grams on the first, second, and third days, respectively, thus showing that with the carbohydrate diet the body of the subject had a tendency to retain a much larger amount of water than with the fat diet. The results of this experiment are presented in table 112.

The chemical analyses of food, feces, and excreta, including especially the determination of carbon dioxide produced, oxygen consumed, and water vaporized, give the data for the exact computation of the kind and amount of material lost from the body. The results from this 6-day experiment show that the quantities of the food had been so adjusted to the needs of the body that there was practically no draft upon body-material or storage of either protein, fat, or carbohydrates, but that there were great changes in the amount of water. It was found on the average that the body actually stored 165 grams of water per day during the carbohydrate period and actually lost on the average 906 grams of water per day during the fat period. This loss during the fat period corresponds almost exactly with the loss in body-weight, and shows that the loss is due to water. Similar experiments have shown that the reverse is true, *i. e.*, when the previous diet contained a preponderance of fat and the change was suddenly made to a carbohydrate diet, there was a marked increase in weight. Obviously, there would be a limit to such retention of water, since the body would not continue indefinitely to accumulate water at the rate of 500 or 600 grams a day, as it would soon become "waterlogged" under these conditions. There is, however, something in the character of a rich carbohydrate diet which seems to demand a larger proportion of water, and this demand is provided for by a storage of water in the body-tissue; when the carbohydrate diet is changed to a fat diet, this water is freely excreted. The restriction of carbohydrate and the increase of fat which are prescribed when diabetic patients are first started upon dietetic treatment duplicate the above

TABLE 112.—*Changes in body-weight due to diet.*

CARBOHYDRATE DIET.

Date and diet.	Food and drink.			Body-weight.	Gain (+) or loss (−).
	Solid matter.	Water.	Total.		
1904.	*gms.*	*gms.*	*gms.*	*kilos.*	*gms.*
Apr. 16	...	....	....	75.086	...
16–17	970	3577	4547	75.443	+357
17–18	966	3553	4519	75.414	− 29
18–19	966	3491	4457	75.269	−145
FAT DIET.					
Apr. 19–20	750	3108	3859	74.319	−950
20–21	745	4150	4896	73.480	−839
21–22	747	4152	4899	72.528	−952

	grams.
Average gain per day, carbohydrate diet	+ 61
Average loss per day, fat diet	−914
Water stored per day, carbohydrate period	+165
Water lost per day, fat period	−906

experiment and the loss of weight which such patients usually undergo at once is thus in part explained. Conversely, a gain in weight almost universally accompanies the oatmeal cure.

That other conditions also play an important rôle in the storage of water in the body has been shown in our extensive experience with diabetics. It has been frequently found that when diabetics are on a strict diet and are given relatively large amounts of sodium bicarbonate to counteract the ever-present tendency to acidosis, there may be a considerable retention of water and consequent increase in body-weight inside of a few days. An abstract of the results with one of the cases (Case A) is given in table 113. The records of the body-weights were made in the early morning before food was taken. Beginning November 6, 20 grams of sodium bicarbonate were given daily, and the results show that while the body-weight, on the morning of November 6, was 49.3 kilos., on the morning of November 11 it had increased to 53.3 kilos., or a gain of 4 kilos. Since at this time the subject was living on a very restricted diet, with barely enough energy in the diet for daily maintenance, it can be seen that this increase must have been due not to the retention of organized body-material, either protein or fat, but simply to water. If the dietetic conditions had been reversed, an equally rapid loss in weight would have been expected, corresponding to the amount of water lost.

TABLE 113.—*Gain in weight of a diabetic with administration of sodium bicarbonate.**

Date.	Sodium bicarbonate.	Body-weight.	Date.	Sodium bicarbonate.	Body-weight.
	gms.	*kilos.*		*gms.*	*kilos.*
Nov. 2.....	0	48 1	Nov. 7...	20	50 7
3.....	0	48 6	8...	20	51 5
4.....	0	49 0	9...	20	52 4
5.....	0	48.6	10...	20	53.3
6.....	20	49.3	11...	20	53.3

*The proportions of protein, carbohydrate, and fat, as well as total calories, were nearly constant throughout.

While a knowledge of the fluctuations in body-weight due to the retention or loss of water plays an important rôle in gaining a correct understanding of the significance of changes in body-weight, we need pay particular attention only to drafts upon organized body-material. Of the four remaining constituents of the body—the protein, fat, carbohydrate, and the mineral matter—the largest addition or depletion can be made in the case of fat. Additions to the protein content of the body are not so easily made as are additions to the fat. Experiments in the laboratory of Professor von Noorden[1] have shown, however, that considerable quantities of nitrogenous material can be stored in the body, but how this is stored and in what form is by no means certain. It is, however, reasonably certain that the protein is not stored in the form of active protoplasmic tissue which necessitates an active metabolism. After the body has been subjected to a fast it seems to have an especial ability to restore the loss of nitrogenous material and even take on a greater amount. While under

[1] See Müller, Zentralblatt f. die ges. Path. u. Pharm. des Stoffwechsels, 1911, 6, p. 617.

special experimental conditions it is possible for us to add to or take from the store of nitrogen in the body to the extent of several hundred grams, nevertheless this is rarely accomplished. Cousequently, in studying fluctuations of body-weight ordinarily occurring outside of those attendant upon wasting diseases, we do not need to consider any alterations in the storage of body nitrogen.

One of the most important compounds in the human body is the relatively small quantity of carbohydrate material, chiefly in the form of glycogen in the liver and muscles. While it is believed that there may be, relatively speaking, a large draft upon this storage of body-glycogen, which has been estimated by some writers to be not more than 400 grams, the total fluctuation one way or the other is not of sufficient moment to play any part in considering the major changes in body-weight. It is possible, indeed probable, that varying amounts of glycogen may indirectly control or influence the presence of varying amounts of water, but glycogen *per se* can not be materially added to the body or taken from the body, since the total storage is small—probably not far from 400 grams. The remaining compound of the body, *i. e.*, fat, can, however, be enormously added to or taken from. It is with changes in the storage or loss of fat that we have chiefly to do when discussing the question of the gains and losses in body-weight, particularly losses that are the result of a progressive change covering some weeks or months.

It has already been pointed out how by certain abnormal conditions we can produce rapid fluctuations in the water-content of the body, but it is practically impossible to secure any rapid change in the amount of fat stored or lost by the body. Even fasting for a day does not lead to any appreciable draft upon the storage of fat. It has been proved that in a normal healthy individual undergoing a complete fast for 24 hours, the glycogen may be depleted to the extent of possibly one-half of its original value. Then after this depletion of glycogen has taken place, the fat is drawn upon, and after the third day the draft is chiefly upon the fat-content of the body, with a relatively small but constant depletion of the glycogen and protein; thus it is seen that any changes in weight having to do with 1 or 2 pounds inside of 24 hours can not in any way be considered as changes in the fat-content of the body.

To study the character of these changes, respiration experiments are essential, in which the carbon-dioxide production is determined as well as the oxygen intake and, if possible, the vaporization of water. If we were to collect all of the products of expiration from the body, namely, the carbon dioxide and water-vapor, we would not even then have an equivalent of the material lost from the body, for of the carbon dioxide and that portion of the water which is formed by the oxidation of organic hydrogen, a not inconsiderable amount is due to the weight of the oxygen absorbed from the air. For instance, assuming that a man at rest in 24 hours produces 700 grams of carbon dioxide and gives off 900 grams of water by sensible and insensible perspiration, this total weight of 1,600 grams does not by any means represent the loss from the body, since of this amount at least 700 grams is due to the oxygen absorbed out of the air, and the actual loss from the body would therefore be approximately 900 grams of water and organic material.

Here again we find the ever-occurring changes in water-content completely masking all information with regard to the loss of organized body-tissue. The water given off from the body is from two sources, first, the preformed water existing as such in the tissues, and, second, the water resulting from the oxidation or burning of organized body-material. The respiration calorimeter with its accessory appliances shows us the method by which the water leaves the body, but it does not tell us whether the water from these two sources has any selective method of discharge; thus, all the water formed from the combustion of organic tissue is not excreted through the lungs and skin, nor is the water drunk all excreted through the kidneys. The data for the losses in gross weight cease to be of any service to us, therefore, in telling us what proportion of the daily loss is due to the oxidation of organized tissue.

As a result of a large number of calorimetric experiments on men, both fasting and with food, it can be shown that the average man at rest without food may oxidize per day about 75 grams of protein, 25 grams of glycogen, and 200 grams of fat, a total of 300 grams of water-free organized body-tissue. It can be readily seen, therefore, that with subjects at rest large changes in weight must be due not to the oxidation of organic matter, which amounts to only 300

TABLE 114.—*Loss in body-weight after severe muscular exercise.*

Subject.	Duration of work.	Loss in weight.	
	hrs. min.	*lbs.*	*kilos.*
Football player	1 10	14.0	6.4
Marathon runner	3 0	8.5	3.9
College 8-oared boat crew	0 22	5.5	2.5

grams per day, but to large excretions of water. With increased muscular activity we have both increased destruction of organized tissue and likewise very large increases in the amount of water lost from the body. This is well shown by the records of losses in body-weight due to the excessive exercise of athletes, and while the observations lack that finality in conclusions that experiments in the calorimeter have, yet they are of great interest. The strenuous exercise incidental to eight-oared boat racing and to football games, particularly in the early fall, when the subjects are not perfectly trained and when the weather is liable to be hot, has frequently been made the subject of more or less observation. Thanks to the kindness of Prof. William G. Anderson, of the Yale University gymnasium, we are able to present authoritative figures on this subject. A number of years ago a well-known football player at Yale was weighed before and after a contest which lasted in all about an hour of actual playing. During the period this man, whose original body-weight was 191 pounds, actually lost 14 pounds. This observation, together with some others likewise furnished by Professor Anderson, are given in table 114. As previously stated, a man sitting quietly loses weight as the result of insensible perspiration approximately 40 grams per hour. The football player lost 6,000 grams, or 150 times as much.

It is impracticable inside the narrow confines of a respiration calorimeter to study the metabolism of Marathon runners or a college eight-oared boat crew, but a bicycle rider, riding to the limit of human endurance, has been studied.[1] If we use the figures for carbon-dioxide production and oxygen consumption determined on this professional rider, we shall be able to compute the probable loss in weight from the body of the football player which was due to the oxidation of organic material; by deducting this loss from the total weight, we can find the loss due to the insensible and sensible perspiration. The bicyclist produced 200 grams of carbon dioxide per hour and absorbed 121 grams of oxygen. Since practically all of the oxygen absorbed was immediately given off in combustion products, we may infer that of the total loss in weight from the body the carbon sufficient to produce 200 grams of carbon dioxide represents approximately the amount of organic material lost from the man's body during one hour of severe muscular work, although there should also be a small allowance for hydrogen. It is safe to say, therefore, that during an hour of exceedingly hard muscular work, such as this strenuous football player indulged in, there would be burned in the body not far from 100 grams of dry organic material. This is approximately a quarter of a pound, leaving a total of 13.75 pounds of lost weight due to water. However, eating and drinking caused the body-weight of the subject to return to normal inside of 48 hours.

This illustration not only serves admirably to show the enormous fluctuations that can take place in the body in a very short time, but also gives us a hint as to the possible cause of sudden changes in body-weight such as may be experienced inside of 24 or 48 hours, namely, that these changes in body-weight must of necessity be due to changes in the water-content and not to changes in the organic constituents of the body. In mild diabetes the initial loss in body-weight may therefore well be due in large part to loss of water, and although there may be a rapid fall in body-weight, sufficient to alarm both patient and physician, it need not necessarily represent the loss of organized tissue; it may simply be due to the restriction of carbohydrate during the process of getting the patient sugar-free. During the initial course of the disease, therefore, changes in body-weight are liable to be peculiarly deceptive, both qualitatively and quantitatively, since an apparent large loss in body-weight may be due exclusively to changes in water-content, with material drafts upon the organized tissues. After this preliminary period with marked loss in body-weight has passed, it is probable that the loss is then due to tissue disintegration.

While it is true that sudden initial changes in body-weight may reasonably be ascribed to fluctuations in the water-content of the body, it nevertheless remains a fact that an inevitable consequence of diabetes, especially when severe, is a persistent and considerable loss in weight. Although it is difficult to obtain accurate data from patients with regard to their greatest body-weight in health, particularly without clothes, we have attempted in all these cases to secure information with regard to this important factor. These weights are given in table 115, together with the minimum weight observed by

[1]Benedict and Carpenter, U. S. Dept. Agr., Office Exp. Stas. Bul. 208, 1909, p. 29.

us or at death. From these the loss in body-weight has been computed, as well as the percentage loss. It is seen that in these cases the loss in body-weight varied from 5.4 to 48.3 per cent of the initial highest body-weight, with an average loss of 22.7 per cent. It is thus clear that a large percentage loss in body-weight is almost regularly observed in severe diabetes.

On some 200 cases taken from several hundred in the practice of one of us (E. P. J.) we have likewise computed the percentage loss in body-weight, using the highest and minimum body-weights observed. These are given in table 116. It so happens that the maximum percentage loss observed in these 200 cases (that of Case No. 3, an excessively fat individual) was but slightly greater than that observed in our Case R, who had an initial body-weight essentially one-half that of Case No. 3. We have also computed the loss in weight experienced by these patients before being seen by E. P. J. as an index of the degree of emaciation which patients usually reach before coming under special treatment for diabetes. It should be borne in mind that these losses in

TABLE 115.—*Comparison of body-weights of subjects in health and disease.*

Subject.	Greatest body-weight in health.	Minimum weight observed.	Loss in body-weight.	Per cent loss of original hest weight.	Subject.	Greatest body-weight in health.	Minimum weight observed.	Loss in body-weight.	Per cent loss of original hest weight.
	kilos.	*kilos.*	*kilos.*	*p. ct.*		*kilos.*	*kilos.*	*kilos.*	*p. ct.*
Case A.......	68.0	46.1	21.9	32.2	Case O.......	60.8	49.2	11.6	19.1
B.......	50.7	37.5	13.2	26.0	P.......	49.9	38.4	11.5	23.0
C.......	73.5	54.9	18.6	25.3	Q.......	54.0	51.1	2.9	5.4
D.......	57.3	45.9	11.4	19.9	R.......	66.7	34.5	32.2	48.3
F.......	80.5	54.5	26.0	32.3	S.......	71.1	57.5	13.6	19.1
G.......	73.6	53.1	20.5	27.9	T.......	71.2	50.6	20.6	28.9
H.......	57.7	49.2	8.5	14.7	U.......	53.1	35.8	17.3	32.6
I.......	56.8	39.3	17.5	30.8	V.......	63.5	58.3	5.2	8.2
J.......	59.1	51.5	7.6	12.9	W.......	63.5	51.7	11.8	18.6
K.......	73.2	55.6	17.6	24.0	X.......	90.7	62.3	28.4	31.3
L.......	79.1	62.2	16.9	21.4					
M.......	86.4	80.6	5.8	6.7	Average...	....	....	....	22.7
N.......	34.5	29.6	4.9	14.2					

weight of diabetic patients are not necessarily the result of a sudden change in 1 or 2 weeks, but usually extend over a period of several months; the only inference that can be drawn is that patients undergoing such losses in body-weight are prone to delay dietetic treatment too long.

The gains in weight of diabetics noted on the administration of sodium bicarbonate or following a change in the diet with the ingestion of large amounts of carbohydrate in the form of oatmeal may be and probably are due wholly to the variations in composition of the water-content of the body; hence such gains are not to be considered as additions to organized body-tissue. The tendency of optimistic patients to consider the gain in weight of a pound or more as an advantageous sign must, in certain instances at least, be dispelled by the attending physician, who should explain that the change in body-weight is probably due to a change in the water-content of the body, and in some cases can demonstrate this by calling attention to the appearance of edema. With the diabetic cases, therefore, we have practically two fundamentally different alterations in body-weight to be considered: first, an initial rapid loss in weight

TABLE 116.—*Losses in body-weight by diabetics.*

[Weights without clothing.]

Case No.	(a) Greatest weight.	(b) Weight at our first observation.	Loss in weight previous to observation. (c) Amount (a−b).	(d) Per cent (c÷a).	(e) Minimum weight observed.	Maximum loss in weight. (f) Amount (a−e).	(g) Per cent (f÷a).
	kilos.	kilos.	kilos.		kilos.	kilos.	
[1]3	110.3	62.3	48.0	43.5	56.5	53.8	48.8
[1]5	113.9	111.2	2.7	2.4	98.5	15.4	13.5
[1]7	64.0	51.1	12.9	20.2	49.1	14.9	23.3
8	79.9	70.8	9.1	11.4	63.8	16.1	20.2
[1]10	86.7	68.6	18.1	20.9	61.8	24.9	28.7
[1]12	64.0	47.8	16.2	25.3	45.4	18.6	29.1
[1]13	91.3	79.5	11.8	12.9	76.1	15.2	16.6
[1]14	86.7	69.0	17.7	20.4	55.4	31.3	36.1
[1]15	61.8	39.1	22.7	36.7	....	....	...
[1]16	98.5	87.0	11.5	11.7	86.3	12.2	12.4
[1]17	71.8	59.5	12.3	17.1	59.5	12.3	17.1
18	73.1	57.2	15.9	21.8	57.2	15.9	21.8
[1]19	95.8	80.0	15.8	16.5	73.6	22.2	23.2
21	63.1	50.6	12.5	19.8	50.6	12.5	19.8
25	63.1	45.3	17.8	28.2	45.3	17.8	28.2
26	109.4	99.9	9.5	8.7	99.9	9.5	8.7
[1]28	39.7	34.2	5.5	13.9	31.8	7.9	19.9
[1]31	30.4	26.8	3.6	11.8	....	....	....
[1]32	82.2	56.7	25.5	31.0	....	....	....
33	95.8	94.9	0.9	0.9	82.0	13.8	14.4
34	65.5	65.5	0	0	61.8	3.7	5.6
[1]36	93.5	83.8	9.7	10.4	78.9	14.6	15.6
37	82.2	67.6	14.6	17.8	67.6	14.6	17.8
[1]38	49.5	45.0	4.5	9.1	45.0	4.5	9.1
[1]39	65.9	59.7	6.2	9.4	57.7	8.2	12.4
[1]40	64.9	55.4	9.5	14.6	38.9	26.0	40.1
[1]41	103.5	75.4	28.1	27.2	75.4	28.1	27.1
[1]42	84.9	68.1	16.8	19.8	61.8	23.1	27.2
[1]44	64.9	56.8	8.1	12.5	49.1	15.8	24.3
[1]45	40.6	34.5	6.1	15.0	34.5	6.1	15.0
46	108.0	79.9	28.1	26.0	79.9	28.1	26.0
[1]48	109.4	74.7	34.7	31.7	72.2	37.2	34.0
49	94.9	82.4	12.5	13.2	82.4	12.5	13.2
[1]51	88.5	65.7	22.8	25.8	60.9	27.6	31.2
[1]52	66.3	50.1	16.2	24.4	49.5	16.8	25.3
[1]54	86.7	49.8	36.9	42.6	48.6	38.1	43.9
[1]55	55.0	52.7	2.3	4.2	52.7	2.3	4.2
[1]56	79.9	61.7	18.2	22.8	61.7	18.2	22.8
[1]57	68.6	56.6	12.0	17.5	55.9	12.7	18.5
59	68.6	59.3	9.3	13.6	55.9	12.7	18.5
[1]62	63.6	46.3	17.3	27.2	46.3	17.3	27.2
[1]64	68.6	48.6	20.0	29.2	42.3	26.3	38.3
65	59.5	58.3	1.2	2.0	58.5	1.0	1.7
[1]66	112.1	89.9	22.2	19.8	87.0	25.1	22.4
70	118.5	107.8	10.7	9.0	103.0	15.5	13.1
71	80.8	78.0	2.8	3.5	78.0	2.8	3.5
[1]72	58.6	55.2	3.4	5.8	50.0	8.6	14.7
[1]73	94.9	77.8	17.1	18.0	73.1	21.8	23.0
75	73.1	58.6	14.5	19.8	58.6	14.5	19.8
76	68.6	55.3	13.3	19.4	54.5	14.1	20.6
77	63.1	44.6	18.5	29.3	42.7	20.4	32.3
78	59.5	55.5	4.0	6.7	53.5	6.0	10.1
[1]79	77.6	60.4	17.2	22.2	53.1	24.5	31.6
[1]81	75.8	60.8	15.0	19.8	60.8	15.0	19.8
[1]82	58.4	49.3	9.1	15.6	49.3	9.1	15.6
83	62.2	54.1	8.1	13.0	54.1	8.1	13.0
84	107.1	79.5	27.6	25.8	73.2	33.9	31.7
[1]85	93.5	56.8	36.7	39.3	56.8	36.7	39.3
89	97.2	77.6	19.6	20.2	73.1	24.1	24.8
[1]91	64.0	51.1	12.9	20.2	44.1	19.9	31.1
92	95.8	82.8	13.0	13.6	78.2	17.6	18.4
93	79.9	64.8	15.1	18.9	62.9	17.0	21.3
[1]94	64.0	48.7	15.3	23.9	47.1	16.9	26.4
97	93.5	75.8	17.7	18.9	72.2	21.3	22.8
99	77.6	67.5	10.1	13.0	65.4	12.2	15.7
100	70.8	63.6	7.2	10.2	63.6	7.2	10.2
[1]101	75.4	55.8	19.6	26.0	55.8	19.6	26.0
102	79.9	71.9	8.0	10.0	66.8	13.1	16.4
103	104.9	95.3	9.6	9.2	75.4	29.5	28.1
[1]105	43.6	41.5	2.1	4.8	41.5	2.1	4.8
107	70.8	44.5	26.3	37.1	44.5	26.3	37.1
[1]108	61.8	61.8	0	0	57.2	4.6	7.4

[1]Dead.

TABLE 116.—*Losses in body-weight by diabetics*—Continued.

Case No.	(a) Greatest weight.	(b) Weight at our first observation.	Loss in weight previous to observation. (c) Amount (a−b).	(d) Per cent (c÷a).	(e) Minimum weight observed.	Maximum loss in weight. (f) Amount (a−e).	(g) Per cent (f÷a).
	kilos.	*kilos.*	*kilos.*		*kilos.*	*kilos.*	
[1]109	39.7	39.1	0.6	1.5	39.1	0.6	1.5
111	116.2	108.8	7.4	6.4	107.7	8.5	7.3
[1]112	104.4	82.6	21.8	20.9	79.6	24.8	23.8
113	82.2	82.4	+0.2	+0.2	82.2	0	0
114	65.9	56.1	9.8	14.9	56.1	9.8	14.9
[1]119	32.0	31.0	1.0	3.1	31.0	1.0	3.1
120	100.3	85.6	14.7	14.7	79.7	20.6	20.5
[1]121	66.3	39.2	27.1	40.9	38.4	27.9	42.1
122	86.7	77.1	9.6	11.1	74.1	12.6	14.5
124	88.5	73.4	15.1	17.1	73.4	15.1	17.1
126	82.2	72.7	9.5	11.6	72.5	9.7	11.8
[1]129	15.2	13.4	1.8	11.8	12.9	2.3	15.1
130	70.4	55.1	15.3	21.7	55.1	15.3	21.7
131	102.6	92.4	10.2	9.9	80.4	22.2	21.6
[1]132	79.0	61.8	17.2	21.8	53.6	25.4	32.2
[1]133	90.3	69.8	20.5	22.7	65.9	24.4	27.0
[1]134	81.7	58.6	23.1	28.3	50.2	31.5	38.6
[1]135	58.6	54.8	3.8	6.5	33.1	25.5	43.5
[1]137	67.2	51.0	16.2	24.1	50.8	16.4	24.4
[1]138	61.8	50.9	10.9	17.6	50.9	10.9	17.6
[1]139	58.6	52.2	6.4	10.9	47.7	10.9	18.6
[1]140	77.6	57.4	20.2	26.0	57.4	20.2	26.0
141	102.6	82.0	20.6	20.1	81.7	20.9	20.4
143	62.7	63.5	+0.8	+1.3	57.2	5.5	8.8
[1]145	76.7	63.8	12.9	16.8	54.1	22.6	29.5
[1]146	60.4	49.8	10.6	17.6	49.8	10.6	17.6
[1]147	79.9	65.5	14.4	18.0	61.0	18.9	23.7
149	53.1	53.4	+0.3	+0.6	53.4	+0.3	+0.6
317	90.7	64.5	26.2	28.9	62.3	28.4	31.3
[1]320	63.5	58.3	5.2	8.2	58.3	5.2	8.2
321	102.6	88.2	14.4	14.0	86.7	15.9	15.5
[1]324	64.0	38.4	25.6	40.0	38.4	25.6	40.0
[1]325	25.2	20.3	4.9	19.4	20.2	5.0	19.8
326	97.1	78.7	18.4	19.0	78.7	18.4	19.0
327	109.4	90.7	18.7	17.1	90.7	18.7	17.1
[1]328	92.2	78.5	13.7	14.9	68.8	23.4	25.4
329	102.6	91.5	11.1	10.8	85.1	17.5	17.1
330	54.1	47.2	6.9	12.8	47.2	6.9	12.8
331	87.2	87.8	+0.6	+0.7	69.0	18.2	20.9
[1]332	53.1	39.7	13.4	25.2	35.8	17.3	32.6
333	63.5	61.1	2.4	3.8	51.7	11.8	18.6
337	112.6	82.2	30.4	27.0	82.2	30.4	27.0
339	69.5	59.3	10.2	14.7	56.3	13.2	19.0
[1]340	76.7	63.8	12.9	16.8	63.8	12.9	16.8
341	64.0	59.8	4.2	6.6	59.6	4.4	6.9
343	99.9	73.6	26.3	26.3	73.6	26.3	26.3
[1]344	66.7	60.5	6.2	9.3	34.5	32.2	48.3
345	77.6	63.8	13.8	17.8	63.8	13.8	17.8
[1]347	68.6	56.6	12.0	17.5	56.6	12.0	17.5
348	73.1	64.4	8.7	11.9	64.4	8.7	11.9
349	79.9	68.2	11.7	14.6	66.2	13.7	17.1
351	82.2	69.9	12.3	15.0	69.9	12.3	15.0
352	86.7	69.0	17.7	20.4	67.8	18.9	21.8
356	98.1	88.2	9.9	10.1	87.0	11.1	11.3
[1]357	95.8	68.1	27.7	28.9	68.1	27.7	28.9
358	102.6	86.6	16.0	15.6	86.6	16.0	15.6
359	70.8	58.7	12.1	17.1	58.7	12.1	17.1
360	84.9	78.8	6.1	7.2	75.7	9.2	10.8
361	68.6	62.1	6.5	9.5	60.4	8.2	12.0
[1]364	45.9	43.4	2.5	5.4	43.4	2.5	5.4
365	41.0	40.9	0.1	0.2	40.9	0.1	0.2
366	64.9	61.7	3.2	4.9	58.5	6.4	9.9
367	49.5	41.4	8.1	16.4	41.4	8.1	16.4
[1]369	104.9	80.4	24.5	23.4	80.4	24.5	23.4
370	65.4	63.5	1.9	2.9	63.5	1.9	2.9
[1]372	60.9	50.7	10.2	16.7	43.1	17.8	29.2
376	84.5	59.1	25.4	30.1	59.1	25.4	30.1
377	31.5	31.0	0.5	1.6	31.0	0.5	1.6
378	80.8	61.7	19.1	23.6	54.7	26.1	32.3
379	93.5	75.8	17.7	18.9	71.8	21.7	23.2
[1]381	71.2	52.7	18.5	26.0	50.6	20.6	28.9
382	44.1	38.0	6.1	13.8	38.0	6.1	13.8
386	84.5	66.8	17.7	20.9	66.8	17.7	20.9
[1]387	55.0	44.8	10.2	18.5	44.1	10.9	19.8

[1] Dead.

TABLE 116.—*Losses in body-weight by diabetics*—Continued.

Case No.	(*a*) Greatest weight.	(*b*) Weight at our first observation.	Loss in weight previous to observation.		(*e*) Minimum weight observed.	Maximum loss in weight.	
			(*c*) Amount (*a*—*b*).	(*d*) Per cent (*c*÷*a*).		(*f*) Amount (*a*—*e*).	(*g*) Per cent (*f*÷*a*).
	kilos.	*kilos.*	*kilos.*		*kilos.*	*kilos.*	
390	69.0	65.4	3.6	5.2	64.5	4.5	6.5
391	73.1	80.7	+ 7.6	+10.4	80.7	+ 7.6	+10.4
392	84.0	78.6	5.4	6.4	70.8	13.2	15.7
394	77.6	63.6	14.0	18.0	61.6	16.0	20.6
[1]396	93.5	82.5	11.0	11.8	82.5	11.0	11.8
398	79.0	82.8	+ 3.8	+ 4.8	82.8	+ 3.8	+ 4.8
399	80.8	64.3	16.5	20.4	63.7	17.1	21.2
[1]400	59.0	45.7	13.3	22.5	40.9	18.1	30.7
401	45.9	45.2	0.7	1.5	45.2	0.7	1.5
402	61.8	55.6	6.2	10.0	46.5	15.3	24.8
403	83.1	64.2	18.9	22.7	64.2	18.9	22.7
405	49.5	47.6	1.9	3.8	46.4	3.1	6.3
408	82.2	55.0	27.2	33.1	55.0	27.2	33.1
409	78.6	77.6	1.0	1.3	76.4	2.2	2.8
411	77.6	78.5	+ 0.9	+ 1.2	78.5	+ 0.9	+ 1.2
413	95.8	68.6	27.2	28.4	68.6	27.2	28.4
[1]414	53.4	43.6	9.8	18.4	43.6	9.8	18.4
420	69.9	63.8	6.1	8.7	63.8	6.1	8.7
421	94.9	76.2	18.7	19.7	76.2	18.7	19.7
424	79.9	63.8	16.1	20.2	63.8	16.1	20.2
428	72.2	70.5	1.7	2.4	70.5	1.7	2.4
429	98.1	68.8	29.3	29.9	68.8	29.3	29.9
430	72.2	54.7	17.5	24.2	51.3	20.9	28.9
431	75.4	69.5	5.9	7.8	69.2	6.2	8.2
432	98.1	80.4	17.7	18.0	80.4	17.7	18.0
[1]433	65.4	46.4	19.0	29.1	41.4	24.0	36.7
434	20.2	18.7	1.5	7.4	18.7	1.5	7.4
435	68.6	56.5	12.1	17.6	56.5	12.1	17.6
436	67.7	65.2	2.5	3.7	63.0	4.7	6.9
[1]439	58.6	45.6	13.0	22.2	45.6	13.0	22.2
[1]440	73.1	57.2	15.9	21.8	54.9	18.2	24.9
442	55.0	58.4	+ 3.4	+ 6.2	58.4	+ 3.4	+ 6.2
443	92.2	78.4	13.8	15.0	78.4	13.8	15.0
444	70.8	61.4	9.4	13.3	61.4	9.4	13.3
445	92.2	86.1	6.1	6.6	86.1	6.1	6.6
447	69.9	70.7	+ 0.8	+ 1.1	70.7	+ 0.8	+ 1.1
448	68.6	55.7	12.9	18.8	55.7	12.9	18.8
449	68.6	53.2	15.4	22.5	49.8	18.8	27.4
450	85.4	83.4	2.0	2.3	79.7	5.7	6.7
451	76.3	44.1	32.2	42.2	41.5	34.8	45.6
452	48.2	40.4	7.8	16.2	35.4	12.8	26.6
453	86.7	61.8	24.9	28.7	58.6	28.1	32.4
454	93.5	65.5	28.0	29.9	61.6	31.9	34.1
455	99.0	96.8	2.2	2.2	96.2	2.8	2.8
[1]456	77.6	65.4	12.2	15.7	65.4	12.2	15.7
457	71.8	69.7	2.1	2.9	61.9	9.9	13.8
459	75.4	71.8	3.6	4.8	71.8	3.6	4.8
462	99.4	100.8	+ 1.4	+ 1.4	96.5	2.9	2.9
464	84.5	61.9	22.6	26.7	61.9	22.6	26.7
466	67.2	67.3	+ 0.1	+ 0.1	67.3	+ 0.1	+ 0.1
467	73.1	64.8	8.3	11.4	64.0	9.1	12.4
469	66.3	53.7	12.6	19.0	53.7	12.6	19.0
472	63.1	54.1	9.0	14.3	51.7	11.4	18.1
[1]473	77.6	58.5	19.1	24.6	58.5	19.1	24.6

[1] Dead.

which is due almost exclusively to a loss of water and may result from a dietetic alteration involving the withdrawal of carbohydrates from the body in an effort to make the patient sugar-free; second, a persistent and regular loss in body-weight covering a period of several months, which is due to a deficient energy supply caused by non-assimilation and an insufficient oxidation of food. The case is furthermore somewhat complicated by the fact that the ingestion of sodium bicarbonate may actually produce a gain in body-weight which is obviously due to stored water; indeed, we have still another complication in the fact that the influence of the retention of sodium chloride in edema may become marked, particularly in cases of diabetes, with defective action of the kidneys.

It is safe to say, therefore, that sudden and rapid fluctuations in body-weight of several pounds may invariably be ascribed to changes in the water-content of the body. Persistent and regular losses in body-weight may be logically considered as conclusive evidence of insufficient available calories in the diet. This insufficiency may be due to a non-assimilation of carbohydrates, or to a defective oxidation of fat resulting in the formation of β-oxybutyric and allied acids. In any event, such a persistent and regular loss shows that the patient is not getting sufficient food for daily maintenance and drafts are being made upon body-material to supply the deficiency.

Nitrogen Excretion of Diabetics without Food.

Inasmuch as certain forms of artificially induced diabetes, such, for example, as pancreatic diabetes in dogs, are accompanied by an increase in the total disintegration of nitrogenous tissue, it is of interest to note to what extent nitrogenous material is broken down and excreted in the body of severe diabetics when food is not being taken. Accordingly, during the period of every experiment without food, the urine was collected usually from the first hour of rising in the morning until the end of the experimental period some time in the middle of the forenoon or later. This sample of urine, which thus represented the urine excreted during the experimental period, was analyzed both for nitrogen and for sugar, and it is evident that the total excretion of nitrogen here may be taken as a measure of the normal excretion of nitrogen of the individual when not actively engaged in processes of digestion.

The determinations of the nitrogen on the basis of milligrams per hour per kilogram of body-weight are given for all the later experiments in table 117. The average value is 8.4 mg. per kilogram per hour. In the first series of experiments, the average for all cases was 9.4 mg. per hour. The average for all the experiments from 1908 to 1912 gave, with diabetics both light and severe, 8.9 mg. of nitrogen per kilogram of body-weight per hour.

In the earlier publication the average for the relatively few normal subjects there used gave 6.85 mg. of nitrogen per hour, and it was explained that the difference between the normal value and that found with diabetics could not by any means explain the enormous increase in metabolism found with these subjects. Since this time a large number of other individuals have been studied and the results obtained with 14 of these, which are given in table 118, show on the average a nitrogen excretion of 6.8 mg. per hour per kilogram of body-weight, a value identical with that given in the earlier report.

As an examination of the various charts will show, the diabetic subjects were not given excessively rich nitrogenous diets, nor, indeed, was the total nitrogen in the urine excessively large in any case. In conformity with the advice of Cantani, Naunyn, and others, we have purposely kept our patients upon a low-protein diet. This has been done hoping thereby to render the task more simple of keeping the urine free from sugar, or at least of keeping the sugar at a low level. The low protein was prescribed not because of the preformed sugar in the protein molecules, but because of the tendency for sugar to

TABLE 117.—*Nitrogen excretion of diabetics per kilogram of body-weight per hour in periods without food, 1910–1911.*

Date.	Hours.	Milli-grams.
Case H:		
Apr. 22, 1910	6	8.4
Case I:		
Feb. 23, 1911	4	9 5
Case M:		
Aug. 17, 1910	3	6 4
Case N:		
Dec. 1, 1910	4	10.4
Dec. 3, 1910	4	8.7
Dec. 5, 1910	4	15.7
Dec. 7, 1910	4	13.7
Dec. 10, 1910	4	10.7
Dec. 12, 1910	4	13.2
Dec. 14, 1910	4	12.1
Average	..	12.1
Case O:		
Sept. 22, 1910	3	6.9
Sept. 23, 1910	2	9.5
Sept. 24, 1910[1]	5	4 2
Average	..	6.9
Case P:		
Sept. 25, 1911	3	12.9
Sept. 29, 1911	3	9.2
Oct. 9, 1911	2	10.4
Oct. 10, 1911[2]	2	10.5
Oct. 16, 1911	3	16 4
Average	..	11 9
Case Q:		
Nov. 19, 1910	4	8.7
Nov. 23, 1910	4	3.7
Average	..	6.2

Date.	Hours.	Milli-grams.
Case R:		
May 12, 1911	3	11 6
Case S:		
May 18, 1910	2	5.5
Case T:		
Feb. 14, 1911	4	8.3
Feb. 16, 1911	1	9.5
Average	..	8 9
Case U:		
May 26, 1910	3	5 6
Mar. 31, 1911	4	8 3
Apr. 2, 1911	3	9 8
June 2, 1911	3	10.1
June 2–3, 1911[3]	8	5.7
Average	..	7 9
Case W:		
May 13, 1910	3	4.9
May 24, 1910	3	3.5
Average	..	4 2
Case X:		
Feb. 28, 1910	5	10.8
Mar. 1, 1910	5	11 5
Mar. 17, 1910	6	7.0
Average	.	9 8
Total average of experiments 1910–1911	.	8.4
Average of experiments 1908–1910	..	9 4
Average of experiments 1908–1911	..	8.9

[1] Nitrogen excreted between $2^h\ 15^m$ and $7^h\ 00^m$ a.m.
[2] Nitrogen excreted between $5^h\ 48^m$ and $7^h\ 52^m$ a.m.
[3] Nitrogen excreted between $10^h\ 30^m$ p.m., June 2, and $6^h\ 25^m$ a.m., June 3.

TABLE 118.—*Nitrogen excretion of normal subjects per kilogram per hour in periods without food.*

Subject.	Body-weight (without clothing).	No. of experiments.	Average nitrogen excretion.	Subject.	Body-weight (without clothing).	No. of experiments.	Average nitrogen excretion.
	kilos.		*mg.*		*kilos.*		*mg.*
F. G. B.	82.5	1	6.7	H. L. H.	59.6	3	7.9
J. R.	70.6	2	6.2	H. F. T.	58.6	2	7.2
Dr. H.	66.3	2	4.8	Dr. S.	58.5	5	5 6
J. J. C.	64 6	14	5.7	D. J. M.	58.1	3	8.6
D. M.	63 4	1	8 7	A. G. E.	56.4	1	4 9
F. M. M.	60.5	6	7.5	V. G.	54.5	8	6.0
L. E E.	60.4	6	8.9	T. M. C.	47.7	3	6.2

be formed from the amino-acid radicles in the protein. It was also felt unwise to increase still further the metabolism, which was already high because of the disease itself. Finally, from a prophylactic point of view, it appeared advisable to spare the overburdened kidneys. On the other hand, we have not attempted to prescribe an excessively low-protein intake, because in an earlier case this was done and apparently with harm to the patient. It would be most

desirable to control the clinical experience of Cantani, Naunyn, von Noorden, and others by experiments upon diabetics with a low-protein and with a high-protein intake, and this we hope at some time to do.

It is important in this connection to note that the protein metabolism of these diabetics was not abnormally great, and hence we have not here to deal with anything approximating an excessive specific dynamic action due to the disintegration of body protein as a result of the disease.

Gaseous Metabolism.

CARBON DIOXIDE EXCRETION IN DIABETES.

The earliest factor in the gaseous metabolism of diabetic patients to be quantitatively measured was the carbon-dioxide production, and this was determined by the Pettenkofer-Voit chamber with great accuracy. The same type of apparatus was used even as late as 1910 by Dubois and Veeder under the direction of Brugsch. As was pointed out in our earlier report, the relationship between the carbon-dioxide excretion and the heat production was so accurately established by our experiments with the calorimeters that the carbon-dioxide measurement acquired thereby a new significance.

In discussing the carbon-dioxide production of diabetics in this report, it seems desirable to present again the observations previously reported,[1] but in this instance emphasizing the average carbon-dioxide production not of all cases, but only of such as were classified as severe. These data are given in table 119, in which the carbon-dioxide production of diabetics in experiments without food is expressed as cubic centimeters per kilogram of body-weight per minute. In the earlier investigations, the chair calorimeter, the bed calorimeter, and the respiration apparatus were used about equally, the variations in the carbon-dioxide production as measured on these different forms of apparatus being shown in the table. As was previously pointed out, the carbon-dioxide production as determined with the bed calorimeter and the respiration apparatus was essentially the same, not only with the single individuals but with the group of individuals. On the other hand, with the chair calorimeter there was a considerable increase in the carbon-dioxide production incidental to the increase in muscular tonus because the subjects were sitting up and showed greater activity in general when inside the chair calorimeter. The values for the moderately severe and light cases of diabetes, although included in table 119, do not need special discussion. The particularly low value found for Case M is obviously influenced by the great body-weight of this subject, who was distinctly fat. On the average, therefore, with severe diabetics, the carbon-dioxide excretion per kilogram of body-weight amounted to 3.53 c.c. per minute of carbon-dioxide with the chair calorimeter, 3.15 c.c. with the bed calorimeter, and 3.18 c.c. with the respiration apparatus. The increase of approximately 10 per cent in metabolism noted in experiments with the chair calorimeter over that in experiments with the bed calorimeter and

[1]Benedict and Joslin, *loc. cit.*, p. 176.

the respiration apparatus is fully in conformity with the increased metabolism noted with normal individuals when changing from a lying to a sitting position.[1]

In the later investigation the subdivision of experiments is almost exclusively between the bed calorimeter and the respiration apparatus, there being but one set of experiments made with the chair calorimeter. The results for all the cases are given in table 120. Special attention is drawn to the average carbon-dioxide excretion of the severe cases. Unlike the results given in the earlier report, the experiments with the bed calorimeter apparently show a considerably higher average value than does the respiration apparatus, *i. e.*, 3.64 c.c. against 3.24 c.c. A close inspection of the figures shows, however, that the value for the bed calorimeter is distinctly affected by the abnormally high values of Cases I and N. It is also due to the fact that in practically no case

TABLE 119.—*Carbon dioxide eliminated per kilogram of body-weight per minute by diabetics in experiments without food, 1908–1910.*

Subject.	Chair calorimeter. Carbon dioxide eliminated.			Chair calorimeter. Average.	Bed calorimeter. Carbon dioxide eliminated.			Bed calorimeter. Average.	Respiration apparatus. Carbon dioxide eliminated.				Respiration apparatus. Average.
Severe diabetes.				*c.c.*				*c.c.*					*c.c.*
Case A	3.38	3.05	3.25	3.28	3.22	....	....	3.22	....	....	....	....	....
	3.37	3.52	3.20										
	3.43	3.03	3.29										
B	....	....	....	....	3.23	....	....	3.23	3.04	2.99	2.99	3.17	3.05
C	3.15	3.22	3.14	3.16	2.95	....	....	2.95	2.79	2.78	2.89	2.60	2.90
	3.22	3.15	3.03						2.82	2.78	3.33	3.04	
	3.14	3.24							3.21	2.92	2.83	2.85	
									2.87				
D	....	....	...	....	....	....	....	....	3.25	3.08	3.00	....	3.11
E	3.40	3.18	....	3.29	....	....	....	....	....	....	....	....	....
F	3.44	....	...	3.44	....	....	....	....	....	....	....	....	....
G	....	....	...	....	3.22	....	....	3.22	....	....	....	....	....
H	....	....	....	....	3.24	3.08	2.94	3.12	3.04	....	....	....	3.04
					3.14	3.19							
I	4.32	4.31	....	4.32	....	....	....	....	....	....	....	....	....
J	3.72	....	...	3.72	....	....	....	....	4.02	3.96	3.48	....	3.82
Av. severe cases	....	....	....	3.53	....	....	....	3.15	....	....	....	....	3.18
Light diabetes.													
Case K	3.10	....	....	3.10	....	....	....	....	2.84	....	....	....	2.84
L	3.53	3.42	3.46	3.46	3.44	....	....	3.44	....	....	....	....	....
	3.42												
M	2.41	2.32	....	2.37	2.57	....	....	2.57	....	....	....	....	....
Av. light cases	....	....	....	2.98	....	....	....	3.00	....	....	....	....	2.84

were experiments made simultaneously with the bed calorimeter and the respiration apparatus. The only exception to this is Case U, where the value of 3.88 c.c. with the bed calorimeter does not differ widely from that found with the respiration apparatus, namely, 3.79 c.c. It should be noted that these averages neither represent an equal number of experiments nor comparison experiments with the same subject in the two different forms of apparatus, and consequently do not in any way vitiate the conclusion drawn from the earlier experiments that the carbon-dioxide production with the same individual is essentially the same whether he is in the bed calorimeter or lying on the respiration apparatus. Of the moderately severe and light cases, Case M was studied both with the bed calorimeter and the respiration apparatus, giving essentially the same results.

[1] Emmes and Riche, Am. Journ. Physiol., 1911, **27**, p. 406.

The somewhat higher value found with the chair calorimeter for Case X over that found with the respiration apparatus is again accounted for by the natural influence of change in position and muscular tonus incidental to sitting up.

For the purpose of securing average figures, the carbon-dioxide production of all diabetic subjects thus far studied by us with the chair calorimeter, bed calorimeter, and respiration apparatus has been collected, averaged, and presented in table 121. On inspecting the average values for the severe cases it is again seen that the results are somewhat complicated by the fact that in the first place the same number of individuals were not studied with all three different forms of apparatus. Secondly, the values found with Case I in the chair calorimeter were obtained nearly a year prior to those found with the same case in the bed calorimeter, during which time the disease had progressed and the subject was in a much more critical state and with an essen-

TABLE 120.—*Carbon dioxide eliminated per kilogram of body-weight per minute by diabetics in experiments without food, 1910–1911.*

Subject.	Chair calorimeter.		Bed calorimeter.		Respiration apparatus.	
	Carbon dioxide eliminated.	Average.	Carbon dioxide eliminated.	Average.	Carbon dioxide eliminated.	Average.
Severe diabetes.		*c.c.*		*c.c.*		*c.c.*
Case A					2.89	2.89
H			3.01	3.01		
I			4.33	4.33		
K					3.27 3.29 3.36	3.31
L					3.08	3.08
N			4.26 3.97 3.97 4.06 4.47 4.10 3.92	4.11		
O					3.14 3.15 2.89	3.06
P					3.69 3.68 3.67 3.96 3.73	3.75
Q			3.42 3.29	3.36		
R			3.51	3.51		
S					2.64	2.64
T			3.32 3.26	3.29		
U			3.88	3.88	3.76 3.71 3.79 3.88	3.79
V					3.42[1]	3.42
Av. severe cases				**3.64**		**3.24**
Moderately severe and light diabetes						
Case M			2.29	2.29	2.41	2.41
W					2.78 2.72	2.75
X	3.53 3.25 2.93	3.24			2.82	2.82
Av. moderately severe and light cases		3.24		2.29		2.66

[1] At $6^h 45^m$ a.m. the subject ate a light breakfast consisting of a 2-egg omelet and a cup of coffee. The experiment began at $9^h 22^m$ a.m., the last period ending at $11^h 10^m$ a.m.

tially higher metabolism, although with considerably less extraneous muscular activity. Probably an average of the results obtained with the bed calorimeter and the respiration apparatus will represent more nearly the grand average of the carbon-dioxide production of subjects with severe diabetes lying quietly at rest. This average value, 3.33 c.c. per kilogram of body-weight, may be taken therefore as the average carbon-dioxide production of subjects with severe diabetes. The number of cases of moderately severe and light diabetes are too few from which to draw any general deductions, although a distinct tendency is shown for the carbon dioxide to be somewhat lower in these cases.

TABLE 121.—*Average carbon dioxide eliminated per kilogram of body-weight per minute by diabetics in experiments without food, 1908–1911.*

Subject.	Chair calorimeter.	Bed calorimeter.	Respiration apparatus.
Severe diabetes.	*c.c.*	*c.c.*	*c.c.*
Case A	3.28	3.22	2 89
B	....	3.23	3.05
C	3.16	2.95	2.90
D	....	....	3.11
E	3.29	....	....
F	3.44	..	....
G	....	3 22	....
H	....	3.10	3.04
I	4 32	4.33	....
J	3.72	....	3.48
K (1910)	....	....	3.31
L (1910)	....	....	3.08
N	.. .	4.11	....
O	....	....	3.06
P	....	....	3.75
Q	....	3.36	....
R	....	3.51	....
S	....	....	2 64
T	....	3.29	....
Severe diabetes—Con.	*c.c.*	*c.c.*	*c.c.*
Case U	....	3.88	3.79
V	....	....	3 42
Av. severe cases	3 54	**3 47**	**3 19**
Av. all expts. with bed calorimeter and respiration apparatus	....	**3.33**	
Moderately severe diabetes.			
Case K (1909)	3 10	...	2 84
L (1909)	3.46	~~2.44~~	....
W	....	....	2.75
X	3.24	....	2.82
Av. moderately severe cases	3 27	~~2.44~~	2.80
Light diabetes.			
Case M	2.37	2.43	2 41

3.44

3.44

OXYGEN CONSUMPTION IN DIABETES.

The quantitative measurement of the oxygen consumption of diabetics has been attempted only by means of the Zuntz-Geppert apparatus,[1] by Weintraud and Laves with the Hoppe-Seyler apparatus,[2] and by us[3] in our earlier investigations.[4] The difficulties incidental to the accurate determinations of the oxygen consumption have precluded a more general measurement. On the other hand, exact determinations of the oxygen used by the subject have greater significance as an index of the calorific output of the body than have the determinations of the carbon-dioxide excretion, especially with normal individuals. With diabetics, as we have shown earlier, particularly with severe cases, the carbon-dioxide determinations, if accurately made, may be considered equally as good an index of the heat production as is the oxygen. Nevertheless it remains a fact that quantitative determinations of oxygen have a special significance and are of unusual importance and interest. Since especial emphasis is laid in this report upon the severity of diabetes, in connection with the discussion of the metabolism during diabetes mellitus we have deemed it advisable in table 122 to present again the oxygen determinations obtained in our earlier investigations, accentuating here the oxygen determinations found with the severe cases rather than the total average.

[1] Leo (1891), Stüve (1894), Nehring and Schmoll (1897), Magnus Levy (1905), Mohr (1907).

[2] Weintraud and Laves, Zeitschr. f. physiol. Chem., 1894, **19**, p. 603.

[3] Benedict and Joslin, Publication No. 136, Carnegie Institution of Washington, 1910.

[4] Two articles have recently appeared giving reports of studies made by Rolly and by Leimdörfer of the oxygen consumption of diabetics. Unfortunately these did not come to our attention until after this report had been sent to the printer, and therefore scant comment only is possible in the proof. Rolly in Leipsic used a modified Benedict respiration apparatus. See Rolly, Deutsch. Archiv f. klin Med., 1912, **105**, p. 494. Leimdörfer in von Noorden's laboratory used the Zuntz-Geppert method. See Leimdörfer, Biochem. Ztschr., 1912, **40**, p. 326.

The agreement between the results found with the bed calorimeter and those with the respiration apparatus is obvious, the greater increase noted with the chair calorimeter being explained in part by the fact that there is an actual increase in the metabolism due to the sitting up in the chair, and in part to the fact that the abnormally high values found with Cases I and J were not accompanied by similar experiments with either the bed calorimeter or the respiration apparatus. From this earlier work, therefore, one can conclude that for subjects with severe diabetes, lying quietly, without food, there is approximately a consumption of 4.22 c.c. of oxygen per minute per kilogram of body-weight.

TABLE 122.—*Oxygen absorbed per kilogram of body-weight per minute in experiments with diabetics without food, 1908–1910.*

Subject.	Chair calorimeter.				Bed calorimeter.				Respiration apparatus.				
	Oxygen absorbed.			Average.	Oxygen absorbed.			Average.	Oxygen absorbed.				Average.
Severe diabetes.				*c.c.*				*c.c.*					*c.c.*
Case A	4.86	4.34	4.38	4.62	4.22	....	....	4.22	....	....	....	....	....
	4.92	4.86	4.50	....	....	....		....	....	....	....	....	
	5.17	4.13	4.44										
B	....	....	....	....	4.42	....	....	4.42	4.27	4.04	4.31	4.47	4.27
C	4.20	4.31	4.72	4.45	4.15	....	....	4.15	4.01	4.44	4.08	3.82	4.23
	4.80	4.55	4.08						4.23	3.93	4.85	4.28	
	4.40	4.54							4.52	4.44	4.19	4.06	
									4.14				
D	....	....	....	....	....	....	....	....	4.44	4.14	4.00	....	4.19
E	4.73	4.32	....	4.53	....	....	....	....	....	....	....	....	....
F	4.66	....	....	4.66	....	....	....	....	....	....	....	....	....
G	....	....	....	....	4.38	....	....	4.38	....	....	....	....	....
H	....	....	....	.	4.34	3.88	3.63	4.07	4.03	....	....	....	4.03
					4.32	4.17							
I	5.65	5.98	....	5.82	....	....	....	....	....	....	....	....	....
J	5.01	....	....	5.01	....	....	..	....	..	....	....	....	....
Av. severe cases	....	....	....	4.85	....	....	. .	**4.25**	....	....	....	....	**4.18**
Light diabetes.													
Case K	4.06		....	4.06	....	....	....		4.04	....	..	. .	4.04
L	4.55	4.58	4.64	4.53	4.41	....	....	4.41	....	....	....	....	....
	4.35												
M	3.09	3.20	....	3.15	3.28	....	....	3.28	....	. .	....	....	. ..
Av. light cases	....	....	....	3.91	....	....	....	3.85	....	...	....	....	4.04

The later experiments were almost exclusively made with either the bed calorimeter or the respiration apparatus. The results obtained in these experiments are given in table 123 herewith. As was pointed out in our discussion of the carbon-dioxide consumption, the agreement between the average results found with the bed calorimeter and the respiration apparatus is not what would be expected, because the abnormally high values of subjects I and N as determined in the bed calorimeter are not accompanied by similar observations on the same subject with the respiration apparatus. Likewise, the recent experiments differ from the earlier investigations chiefly in the fact that with practically no subject were experiments made with both the bed calorimeter and the respiration apparatus; therefore the comparison is obviously not as simple as it was in the earlier report. If we consider the average of the results found with the cases of severe diabetes in the bed calorimeter and on the respiration apparatus as representing the truest average, we may state that with these subjects lying quietly at rest without food, 4.73 c.c. of oxygen are

absorbed per kilogram of body-weight per minute. The paucity of experimental data with regard to light cases prevents any general deduction, although it is again obvious that there is on the average a much smaller oxygen consumption per kilogram of body-weight than with the severe cases. Finally, it should be noted that in the experiment with Case X, the value found with the chair calorimeter (4.17 c.c.) is higher than that found with the respiration apparatus (3.79 c.c.) and can be wholly explained by the difference in the muscular activity incidental to experiments in the chair calorimeter.

TABLE 123.—*Oxygen absorbed per kilogram of body-weight per minute by diabetics in experiments without food, 1910–1911.*

Subject.	Chair calorimeter.		Bed calorimeter.		Respiration apparatus.	
	Oxygen absorbed.	Average.	Oxygen absorbed.	Average.	Oxygen absorbed.	Average.
Severe diabetes.		c.c.		c.c.		c.c.
Case A	....	....	....	....	4.08	4.08
H	....	....	3.97	3.97	....	....
I	....	....	6.03	6.03	....	....
K	....	....	....	....	4.62 4.57 4.77	4.65
L	....	....	....	....	4.23	4.23
N	....	....	5.74 5.25 5.39 5.50 5.88 5.71 5.54	5.57	....	....
O	....	....	....	....	4 28 4.44 4.01	4.24
P	....	....	....	....	5.26 5.24 5.40 5 60 5 22	5.34
Q	....	....	4.51 4.23	4.37	....	....
R	....	....	4.90	4.90	....	....
S	....	....	....	....	3.67	3 67
T	....	....	4.66 4.35	4.51	....	....
U	....	....	....	....	4 95 5 21 5 15 5.47	5.20
V	....	....	....	....	4.72[1]	4.72
Av. severe cases	....	....	....	**4 89**	....	**4.57**
Moderately severe and light diabetes.						
Case M	....	....	2.93	2.93	3.21	3.21
W	....	....	....	....	3.91 3 62	3.77
X	4.80 4.08 3.62	4.17	....	....	3 79	3.79
Av. moderately severe and light cases	....	4.17	....	2 93	....	3.59

[1]At $6^h 45^m$ a.m. the subject ate a light breakfast consisting of a 2-egg omelet and a cup of coffee. The experiment began at $9^h 22^m$ a.m., the last period ending at $11^h 10^m$ a.m.

In table 124 are given the averages of the values found in both series of experiments with the different subjects and with the different forms of experimental apparatus, *i. e.*, the bed calorimeter, chair calorimeter, and respiration apparatus, these showing that 4.85 c.c. of oxygen were absorbed and measured in the chair calorimeter, 4.66 c.c. with the bed calorimeter, and 4.41 c.c. with the respiration apparatus. Admitting that the chair-calorimeter results are affected somewhat by increased muscular activity incidental to experiments in this apparatus, we may average the results found in the bed calorimeter and the respiration apparatus and consider the average value of 4.54 c.c. per minute as the best average value for severe diabetics lying quietly at rest without food. The subjects with moderately severe and light diabetes have relatively less oxygen consumption under the same conditions, although in this discussion attention is particularly directed to the values found with the severe cases.

TABLE 124.—*Average oxygen absorbed per kilogram of body-weight per minute in experiments with diabetics without food, 1908–1911.*

Subject.	Chair calorimeter.	Bed calorimeter.	Respiration apparatus.
Severe diabetes.	*c.c.*	*c.c.*	*c.c.*
Case A	4.62	4.22	4.08
B	....	4.42	4.27
C	4.45	4.15	4.23
D	....	....	4.19
E	4.53	....	....
F	4.66	....	....
G	....	4.38	....
H	....	4.05	4.03
I	5.82	6.03	....
J	5.01	....	4.54
K (1910)	....	....	4.65
L (1910)	....	....	4.23
N	....	5.57	....
O	....	....	4.24
P	....	....	5.34
Q	....	4.37	....
R	....	4.90	....
S	....	....	3.67
T	....	4.51	....
Severe diabetes—Con.	*c.c.*	*c.c.*	*c.c.*
Case U	....	....	5.20
V	....	....	4.72
Av. severe cases	4.85	4.66	4.41
Av. all expts. with bed calorimeter and respiration apparatus	....	4.54	
Moderately severe diabetes.			
Case K (1909)	4.06	....	4.04
L (1909)	4.53	4.41	....
W	....	....	3.77
X	4.17	....	3.79
Av. moderately severe cases	4.25	4.41	3.87
Light diabetes.			
Case M	3.15	3.11	3.21

RESPIRATORY QUOTIENT.

The relationship between the volume of carbon dioxide produced and oxygen consumed $\left(\frac{CO_2}{O_2}\right)$, the so-called respiratory quotient, has peculiar significance in interpreting the degree of severity in cases of diabetes. The accuracy of this value depends upon the accuracy of both the determination of carbon dioxide and the determination of oxygen, and it can thus be seen that the respiratory quotient as such is a difficult matter to determine with great exactness. In the earlier report the respiratory quotient for all the cases of diabetes was considered in detail and in table 125 we have presented anew the earlier work, carefully distinguishing between the severe cases and the lighter cases.

In recording the results for the respiratory quotient, it is unnecessary to consider separately those obtained with the three forms of apparatus, for there is no physical difference in the respiration in either the chair or the bed calorimeter, and obviously the character of the combustion and the material burned or metabolized will not be appreciably altered by different body positions. On the other hand, it is reasonable to suppose that the carbon-dioxide production and oxygen consumption might indicate a difference in the character of the combustion, according to whether the subject breathed freely in the calorimeter, or whether he breathed into the nosepieces or mouthpiece of the respiration apparatus. Accordingly, in giving the results of the earlier experiments, the values obtained with the calorimeter are compared with those obtained with the respiration apparatus. It can be seen that the respiratory quotient in the severe cases of diabetes averages 0.74 with the calorimeter and 0.73 with the respiration apparatus. The fact that there are not an equal number of experiments made with the same subject on both apparatus complicates some-

what the comparison. Particularly is this true with subjects having light diabetes with whom an average quotient of 0.76 was obtained in the chair calorimeter, while apparently a quotient of 0.70 was found with the respiration apparatus. An examination of the figures shows, however, that the second value depends wholly upon a single experiment with Case K, and hence as an average value is very much to be questioned. The important thing to be emphasized here is the fact that there were no abnormal quotients found, although a single value of 0.64 was found with Case C and one of 0.66 with Case A. In general, however, none of the abnormally low quotients which have frequently been cited by earlier writers were found; at least there was no persistent evidence of an abnormal katabolism which such low quotients would indicate.

TABLE 125.—*Average respiratory quotients in experiments with diabetics without food, 1908–1910.*

Subject.	Calorimeter.					Respiration apparatus.					
	Respiratory quotient.				Average.	Respiratory quotient.					Average.
Severe diabetes.											
Case A	0.75	0.75	0.74	0.76	0.71	....	....	....	....	....	....
	0.68	0.72	0.71	0.66							
	0.73	0.74									
B	0.74	....	....	....	0.74	0.71	0.75	0.70	....	....	0.72
C	0.75	0.75	0.67	0.69	0.71	0.70	0 64	0.71	0 68	0.67	0.69
	0.69	0.74	0.71	0.71		0.71	0.69	0.71	0.71	0.66	
	0.72					0.68	0.70	0.69			
D	....	....	....	....	....	0.73	0.74	0.75	....	....	0.74
E	0.72	0.74	....	....	0.73	....	....	....	....	....	....
F	0.74	....	....	....	0.74	....	....	....	....	....	....
G	0.73	....	....	....	0.73	....	....	....	....	....	....
H	0.75	0.79	0.81	0.72	0.77	0.76	....	....	....	....	0.76
	0.76										
I	0 76	0.72	....	....	0.74	....	....	....	....	....	....
J	0.75	....	....	....	0.75	....	....	....	....	....	....
Av. severe cases	....	....	....	....	0.74	....	....	....	....	....	0.73
Light diabetes.											
Case K	0.76	....	....	....	0.76	0.70	....	....	....	....	0 70
L	0.78	0.75	0.75	0.78	0.77	....	....	....	....	....	....
	0.79										
M	0 78	0.78	0.72	....	0 76	....	....	....	....	....	....
Av. light cases	....	....	....	....	0.76	....	....	....	....	....	0.70

It should be pointed out again that the respiratory quotient is entirely independent of the total metabolism, and indicates only the character of the metabolism and not the total amount. When the body is subsisting chiefly upon carbohydrates, the respiratory quotient approximates 1. When it is subsisting chiefly upon fat, the respiratory quotient approximates 0.71. The quotients, therefore, here observed with severe diabetes indicate a combustion which is chiefly that of fat. Inasmuch as the relatively small amounts of protein burned tend to raise the quotient, we find the average values slightly above 0.71 rather than slightly below.

The respiratory quotients for the new series of experiments are given in table 126. These quotients, which are classified as severe cases and moderately severe and light cases, indicate again a low respiratory quotient as the characteristic of severe diabetes, the average quotient found with the calori-

meter being 0.73 and with the respiration apparatus 0.72, values not appreciably different from those obtained in the earlier series. As a matter of fact, the lowest individual respiratory quotient found in the new series of experiments was the value 0.68 obtained with Case P in one experiment.

The moderately severe and light cases are too few in number for us to draw any deductions, but there is a tendency for the respiratory quotient to be somewhat higher with the light cases than with the severe, thus indicating a slightly higher combustion of carbohydrate. The low averages found with the severe cases indicate a combustion almost exclusively of fat, with a relatively small amount of protein and almost no carbohydrate combustion. This is

TABLE 126.—*Average respiratory quotients in experiments with diabetics without food, 1910–1911.*

Subject.	Calorimeter.		Respiration apparatus.	
	Respiratory quotient.	Average	Respiratory quotient.	Average.
Severe diabetes.				
Case A	....	....	0.71	0.71
H	0.76	0.76	....	....
I	0.72	0.72	....	....
K	....	....	0.71 0.73 0.71	0.72
L	....	....	0.73	0.73
N	0.74 0.76 0.73 0.74 0.76 0.72 0.71	0.74	....	....
O	....	....	0.74 0.71 0.72	0.72
P	0.69	0.69	0.70 0.70 0.68 0.71 0.71	0.70
Q	0.76 0.78	0.77	....	....
R	0.72	0.72	....	....
S	....	....	0.73	0.73
T	0.71 0.75	0.73	....	....
U	0.73[1]	[1]0.73	0.76 0.71 0.74 0.71	0.73
V	....	....	0.73[2]	0.73[2]
Av. severe cases	....	0.73	....	0.72
Moderately severe and light diabetes				
Case M	0.78	0.78	0.75	0.75
W	....	....	0.72 0.75	0.74
X	0.73 0.80 0.81	0.78	0.74	0.74
Av. moderately severe and light cases	....	0.78	....	0.74

[1]The respiratory quotient for this experiment was for the periods $11^h\ 55^m$ p.m. to $1^h\ 27^m$ a.m. and $5^h\ 05^m$ to $6^h\ 05^m$ a.m., June 2–3, 1911.

[2]At $6^h\ 45^m$ a.m. the subject ate a light breakfast consisting of a 2-egg omelet and a cup of coffee. The experiment began at $9^h\ 22^m$ a.m., the last period ending at $11^h\ 10^m$ a.m.

fully in conformity with the very low carbohydrate supply in the bodies of diabetics, and it is fully in accord with what theoretically would be predicted. Here again we find a complete absence of the abnormally low quotients frequently reported by earlier writers.

In order to sum up the results of all the experiments thus far made, we have computed the respiratory quotients for each individual case both in the calorimeter and with the respiration apparatus when experiments with both apparatus had been made, and they are combined in table 127. It is seen that the average value with severe diabetes in both the calorimeter experiments and the respiration experiments was 0.73, although here again it should be pointed out that experiments on each individual were rarely performed with both apparatus.

It may be concluded, therefore, that with the subject lying quietly without food the respiratory quotient in cases of severe diabetes is 0.73; as pointed out in the earlier report, respiratory quotients carefully determined that indicate values higher than this are to be considered a favorable prognostic indication, and show a rather more liberal supply of carbohydrate material in the body than is usual in severe diabetes.

The difficulties incidental to determining accurately the respiratory quotients are only too well known to experimenters, and hence it would be entirely incorrect to lay great stress upon individual figures in this series. The general tendency of all the quotients to approximate the value 0.73 is significant, as is likewise the absence of abnormally low quotients.

TABLE 127.—*Average respiratory quotients in experiments with diabetics without food, 1908–1911.*

Subject.	Calorimeter.	Respiration apparatus.	Subject.	Calorimeter.	Respiration apparatus.
Severe diabetes.			*Severe diabetes*—Con.		
Case A	0.71	0.71	Case T	0.73	....
B	0.74	0.72	U	0.73	0.73
C	0.71	0.69	V	..	0.73
D	....	0.74			
E	0.73	....	Av. severe cases	**0.73**	**0.73**
F	0.74	....	*Moderately severe diabetes.*		
G	0.73	....			
H	0.77	0.76			
I	0.73	....	Case K (1909)	0.76	0.70
J	0.75	0.77	L (1909)	0.77	
K (1910)	....	0.72	W		0.74
L (1910)	....	0.73	X	0.78	0.74
N	0.74	....			
O	....	0.72	Av. moderately severe cases	0.77	0.73
P	0.69	0.70			
Q	0.77	....	*Light diabetes.*		
R	0.72	....			
S	...	0.73	Case M	0.77	0.75

INDIRECT CALORIMETRY.

Although, as pointed out on page 12, the direct heat measurement in this series of experiments was unsatisfactory in a large majority of the cases, it is important to record that in one-third of the experiments in which accuracy in the heat measurements is assured, the relationships between the oxygen consumption, carbon-dioxide production, and heat production are essentially those recorded in the earlier publication. We have, therefore, no reason to change our belief that the calorific equivalents of carbon dioxide and oxygen are essentially as previously outlined, namely, 3.26 calories per gram of carbon dioxide and 3.31 calories per gram of oxygen. If, then, in experiments with subjects having severe diabetes, the carbon-dioxide production is accurately determined, we believe that the heat production can be computed with considerable accuracy by multiplying the total carbon-dioxide production in grams by the factor 3.26.

Usually, since the carbon-dioxide production is obtained with the subject absolutely quiet, lying in bed, it can be easily seen that the results obtained by this computation will represent the minimum heat production and not the average or maximum heat production. When the subject is sitting up it has

been shown that there is essentially an increased heat production amounting to 10 or 15 per cent.[1] Walking and all muscular activity, also the partaking and the digestion of food, produce an increase in the heat production. The difference in heat production measured on the same subject in the chair calorimeter and in the bed calorimeter is further evidence of the difference in energy output. A careful record of daily routine, muscular activity, exposure to cold, etc., would be necessary for the intelligent computation of the total output of energy from the carbon-dioxide production. It is not outside the range of possibilities that this factor may be of actual benefit in making a tentative computation of the energy requirement in diabetes. That this carbon-dioxide production can be determined equally as well by the small respiration apparatus as with the large respiration calorimeter has, we think, been fairly demonstrated, and we may conclude from this research that, although calorimetric measurements are highly important and desirable if possible, in severe diabetes a measurement of the carbon-dioxide production alone, or still better a measure of the oxygen consumption, will give the means for computing with great accuracy the heat production of the individual while lying quietly at rest.

COMPOSITION OF THE ALVEOLAR AIR OF DIABETICS.

The carbon-dioxide tension of the alveolar air has come to be regarded as an excellent index of the degree of acidosis by reason of the interesting observations of Beddard, Pembrey and Spriggs[2] and the confirmatory work of Porges, Leimdörfer and Markovici.[3] The presence of acids in the blood causes the respiratory center to respond to a smaller tension of carbon dioxide in the blood; as the carbon-dioxide tension in the alveolar air bears a direct relation to that in the blood, it is evident that a low alveolar carbon-dioxide tension indicates an acidosis. The alveolar carbon dioxide in normal individuals varies from about 36 to 46 mm. tension of mercury as found by the Haldane method;[4] according to results obtained by the Plesch method[5] it is about 10 to 15 per cent higher.

The best method for determining the alveolar air has not yet been thoroughly established. Both the Haldane and Plesch methods involve good gas analysis technique and not a little cooperation on the part of the subject.

Alveolar air determinations were made on three of the subjects, N, Q, and I, and are interesting as showing the presence and degree of acidosis. The observations made with Cases N and Q were by the Haldane method; those with Case I were by the Plesch method. The results obtained with Case N are given in table 128.

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[1]Emmes and Riche, Am. Journ. Physiol., 1911, **17**, p. 406.
[2]Beddard, Pembrey and Spriggs, Journ. Physiol., **37**, Proceedings Physiol. Soc., 1908, p. xxxix.
[3]Porges, Leimdörfer and Markovici, Zeitschr. f. klin. Med., 1911, **73**, p. 389.
[4]Haldane and Priestley, Journ. Physiol., 1905, **32**, p. 225.
[5]Plesch, Zeitschr. f. Exp. Pathol. u. Ther., 1909, **6**, p. 380. The Plesch method, in fact, gives the carbon-dioxide tension of the venous blood, but we have found that this value bears a proportional relation to the alveolar air.

On several occasions observations were also made with this case of the rate of respiration, and the total ventilation of the lungs, the results being included in the table. Two observations were likewise made of the blood-pressure (Riva Rocci), one at $7^h\ 30^m$ a. m. December 12, and the second at $7^h\ 10^m$ a. m. December 14; both gave a result of 90 mm. It will be seen that on December 10, when the alveolar carbon-dioxide tension was lower and presumably the acidosis greater than on December 14, there was also an increased ventilation of the lungs. The respiration rate, however, did not vary with the alveolar air or with the ventilation of the lungs.

TABLE 128.—*Determinations made on alveolar air with Case N.*

Date.	Time.	Tension of— Carbon dioxide.	Tension of— Oxygen.
1910.		*mm.*	*mm.*
Dec. 1	After expt., $10^h\ 25^m$ a.m.	17.4	122.3
		16.7	123.8
Dec. 2	Before expt., 8 a.m.	16.4	126.6
		21.1	.....
	After expt., $11^h\ 15^m$ a.m.	22.1	119.2
		21.7	.....
Dec. 3	Before expt., $7^h\ 15^m$ a.m.	25.6	.....
		25.3	.....
	After expt., $10^h\ 30^m$ a.m.	27.2	118.3
		26.8	.....
Dec. 5	Before expt., $7^h\ 20^m$ a.m.	22.2	122.0
		24.2	117.7
	After expt., $10^h\ 45^m$ a.m.	23.5	122.4
		24.1	120.1
Dec. 7	Before expt., $7^h\ 15^m$ a.m.	19.7	.....
		18.3	.....
	After expt., $10^h\ 40^m$ a.m.	22.1	.....
		21.1	.....

Date.	Time.	Tension of carbon dioxide.	Ventilation of lungs, time required for 10 liters.[1]	Respiration per minute.
1910.				
Dec. 10	Before expt.:	*mm.*	*secs.*	
	$7^h\ 20^m$ a.m.	18.6	...	..
		18.9	...	..
	7 30 a.m.	....	73	19
		....	76	19
	7 31 a.m.	....	73	18
	After expt.:			
	$10^h\ 50^m$ a.m.	18.9	...	..
		17.3	...	..
		....	75	22
		....	68	22
	11 01 a.m.	....	76	22
Dec. 12	Before expt.:			
	$7^h\ 15^m$ a.m.	28.5	...	..
		26.9	...	..
	7 22 a.m.	....	111	19
		....	119	18
	7 26 a.m.	....	117	16
	After expt.:			
	$10^h\ 50^m$ a.m.	28.9	...	..
		28.9		.
	11 00 a.m.	...	105	22
	11 01 a.m.	...	121	23
	11 02 a.m.	...	[2]75	21
		...	.	22
	11 05 a.m.	...	...	19
Dec. 14	Before expt.:			
	7 15 a.m.	24.9	...	..
		25.4		..
	7 25 a.m.	...	109	16
		...	112	18
	After expt.:			
	$10^h\ 40^m$ a.m.	26.9	...	..
		26.1		..
	10 51 a.m.	...	120	18
	10 54 a.m.	...	141	14
		...	[2]64	..

[1]At room temperature and observed barometric pressure. [2]Time required for 5 liters.

On each of the four experimental days with Case Q, the carbon-dioxide tension of the alveolar air was determined after the respiration experiments. The results are given in table 129. On November 19 the subject had taken no breakfast previous to the experiment, but the two experiments on November 21 and 22 followed an oatmeal breakfast, while that on November 23, although the subject was without breakfast, followed two oatmeal days. It is interesting to note that the carbon-dioxide tension is very much lower on the 19th than it is on the 23d, indicating a greater acidosis on the former day; the experimental evidence also shows that the metabolism was considerably higher on

the 19th than it was on the 23d after the two oatmeal days. Further reference will be made to these two days in the discussion of the question of the relationship between the acidosis and the severity of the diabetes and intensity of the metabolism.

TABLE 129.—*Determinations made on alveolar air with Case Q.*

Date.	Diet previous to experiment.	Carbohydrates in diet on day preceding.	Time.	Tension of— Carbon dioxide.	Oxygen.
1910.		*gms.*		*mm.*	*mm.*
Nov. 19.....	Without breakfast ..	55	After experiment.	{30.6 / 32.9}	108.7 / .....
Nov. 21.....	Oatmeal breakfast...	55	After experiment.......	{34.6 / 29.5}	..... / .....
Nov. 22.....	Oatmeal breakfast...	165	After experiment.......	{35.8 / 39.7}	..... / .....
Nov. 23.....	Without breakfast, following 2 oatmeal days.	165	After experiment... ...	{40.3 / 40.2}	94.7 / .....

During the short sojourn of Case I at the hospital in February 1912, when he was in a very critical condition and coma was impending, a number of observations were made on the carbon-dioxide tension of the alveolar air in which the subject breathed the same air several times in and out of a rubber bag. In these experiments the subject first inspired 600 c.c. of air, breathing it back

TABLE 130.—*Determinations made on alveolar air with Case I.*

Date and time.	Tension of carbon dioxide.	Pulse per minute.	Respiration per minute.	Remarks.
	mm			
Feb. 14, 1912:		...		Impending coma.
11h 07m a.m ...	29.1			
11 15 a.m.....	25.6		18	
11 30 a.m	27.1	110		
11 40 a.m......	27.3	...		After taking sodium citrate. Very little could be taken because of diarrhea resulting from it.
11 47 a.m.......	..	..	18	Respirations heard and counted from across room.
2 34 p.m.......	....	114	..	Still impending coma. Had been up in a wheel chair for a few moments at noon.
2 39 p.m.......	24.8	...		
2 50 p.m.......	....	...	19	
2 53 p.m.......	26.5	...		Drew in some air around mouth while inspiring.
2 58 p.m.......	26.3	...		Between 12 noon of Feb. 14 and 7 a.m. Feb. 15, the subject took 90 grams of levulose. Still conscious; was very restless during the night.
Feb. 15, 1912:				
8h 03m a.m.......	....	...	19	
8 10 a.m.......	21.0	...	..	
8 20 a.m.......	17.5	...	..	
8 35 a.m.......	22.4	...	..	Took some sodium citrate at 8h 30m a.m.; none previous since 2h 30m a.m.
8 47 a.m.......	....	118	..	
8 48 a.m.......	21.4	...	..	
9 00 a.m.......	....	...	21	
5 00 p. m. about	{20.6	...	..	Dressed, ready to go home. Still breathing heavily; probably no better.
	19.5}	...	..	Had bad morphine in afternoon.

and forth four times in 20 seconds. The last expiration was analyzed for carbon dioxide. The values obtained are given in table 130, together with a few records of the pulse and respiration rates.

This subject was characterized by an abnormally high pulse-rate running from 110 to 118; although the respiration-rate was not extraordinarily high,

averaging not far from 19 per minute, the deep breathing of impending coma was very noticeable, the respirations being easily counted from across the room with one's back to the subject. A gradual fall in the carbon-dioxide tension will be noticed during the two days on which experiments were made. Between noon of February 14 and 7 a. m. of February 15 the subject took 90 grams of levulose, but this seems to have had no effect on the carbon-dioxide tension in the alveolar air.

Comparison of the Metabolism of Diabetics with that of Normal Individuals.

One of the difficulties hitherto encountered in the interpretation of experiments on the metabolism of diabetic patients has been the lack of sufficient controls with normal individuals. In our previous report we were able in a measure to supply this deficiency, and, we believe, presented enough data regarding normal individuals to establish a satisfactory base-line for comparison. Criticism, however, has arisen not only as to the character of the normals selected, but also as to the number. Lusk,[1] whose opinion on matters of diabetes is not to be regarded lightly, maintained that the normal individuals weighed very much more than did the diabetics and hence were not comparable on the basis of per kilogram of body-weight. In the second place, Lusk laid a great deal of stress upon the fact that one of the subjects, Case I, was extremely high-strung, nervous, and apprehensive, and by no means an ideal subject. He maintained that the results with this individual played too important a rôle in our determination of the apparent increase in metabolism. Leaving out of consideration the heavy individuals used in the normal comparison, and omitting, also, the results obtained with Case I, he computed that the increase in the heat production was but 5 per cent instead of the 15 per cent that we maintained.

At the time of going to press with the first diabetic publication, the number of normal individuals available for comparison was somewhat limited, and it was obviously desirable to increase this as rapidly as possible. Fortunately in the intervening time we have been able to study a sufficiently large number of normal individuals so as to extend the list, and are now prepared to meet this criticism by presenting data based on (1) an enlarged number of normal subjects, and (2) a normal individual corresponding in height and weight for all of the diabetics save one. We also have normals to correspond with two diabetics during the several stages of their disease when their weight changed. While, therefore, in the first report the comparisons were made between normal individuals collectively and diabetic individuals collectively, we shall attempt in this publication to compare each diabetic with one or more normal individuals with essentially the same body-weight and height, and finally, as before, to compare normals and diabetics collectively. Under these conditions the criticism of Professor Lusk can be much better met than it could have been two years ago, when the normal data were limited. That Professor Lusk's

[1] Lusk, *loc. cit.*

criticism was more of a theoretical than a practical nature is demonstrated by the fact that the actual increase in metabolism noted in the new observations is somewhat higher than that noted when the earlier tests were made.

The measurements of the metabolism of Case I were stated in the first report to be unsatisfactory for the reason that the subject was high-strung and nervous, and consequently by no means an ideal subject. Fortunately, some months later it was possible to secure this subject for another experiment. At this time he was weak, emaciated, and disinclined to muscular activity. During the experimental period he lay in the bed calorimeter extremely quiet, and prior to the experiment exhibited none of the nervousness and excitement which he had shown before the two experiments of the year previous. These later results may accordingly be taken as a measurement of the metabolism of a diabetic with severe acidosis, but with a minimum amount of extraneous muscular activity. While, therefore, in the earlier experiments with the chair calorimeter he did not appear to be an ideal subject, in his last experiment with the bed calorimeter no criticism could be raised with regard to the conduct of the experiment or to the subject himself, so that the influence of extraneous muscular activity may be disregarded. The results of the last experiment with the subject abundantly confirm those of the first two in showing a marked increase in the total metabolism.

SELECTION OF CONTROLS.

In this comparison of normal individuals with diabetics care has been taken to select controls that approximate as nearly as possible the exact body-weight and height of the diabetic subjects to which they are to be compared. This has been difficult in certain instances, owing to the fact that frequently the diabetics were much emaciated and it was difficult to find a person of a corresponding height and weight. The evidence with regard to the disproportion between skin area and body-weight, first suggested by Magnus-Levy and considered by us in the earlier publication, has been further amplified by observations during an experiment with prolonged inanition. Although during this experiment the subject lost in weight 15 kilograms, there was no loosening of the skin. The skin contracted as the flesh disappeared and hence there was no evidence that there was a disproportion between the body-surface and the body-weight.

A further precaution was taken to select normal subjects who were not on the laboratory staff, except when it was necessary in order to obtain subjects that were comparable in size and weight. Of the 20 or more subjects used for comparison, more than half did not belong to the laboratory staff; hence, on the whole, the normal subjects were more often untrained than were the diabetics with most of whom experiments were frequently made.

EVIDENCE OF THE KYMOGRAPH RECORDS.

The use of one or more tube pneumographs about the thighs or chest for a record of the degree of muscular activity of the subject has proved a most successful venture, but the expense incidental to reproducing kymograph records makes it impossible to present them here. A most careful scrutiny of the

large number of kymograph records obtained in connection with this research makes it evident that the normal individuals on the whole were considerably more restless than were the diabetic individuals. The diabetic patients were for the most part sick, weak, and disinclined to any extraneous muscular movements and remained lying quietly in bed. It may therefore be safely stated that the influence of extraneous muscular activity was infinitely less with the diabetics than with the normal individuals. Hence one would expect to find a higher metabolism with the normal individuals than with the diabetics, as the influence of even minor muscular activity upon the metabolism is surprising—a fact only appreciated by one who is constantly working in the laboratory, measuring the metabolism of a subject and comparing the simultaneous records of muscular activity. This relationship between minor muscular activity and metabolism has been observed in this laboratory,[1] even with infants.

In an experiment designed to answer a criticism as to the soundness of using kymograph records to indicate muscular rest, it was found by actual test that the kymographs are so sensitive that even a minute muscular tremor, such as the movement incidental to slight shivering, is instantly transmitted to the tambour and recorded on the kymograph.

DETAILED COMPARISON OF NORMALS AND DIABETICS.

From our list of normal subjects it is possible to select for purposes of comparison one or more to compare with each individual diabetic, with the single exception of Case N. As he was a boy, we had no normal subject who was comparable in age, weight, and height; consequently, Case N is not included in the averages. On one occasion Case A weighed 51.6 kilos., and later weighed 46.1 kilos.; a fall in body-weight of 7 kilos. was likewise noticed with Case C. Accordingly, in order to make the analogy as complete as possible, we have compared the diabetics with different normals at the stages of the disease when there was a change in their body-weights. All these comparisons have been brought together in table 131, in which are grouped first, the cases of severe diabetes and the normal individuals with whom they are compared, and second, the moderately severe and light cases, of which only three were studied. Of particular interest are the comparisons between the cases of severe diabetes and the normal individuals.

The carbon-dioxide production per kilogram of body-weight with all of the cases of severe diabetes was 3.31 c.c. per kilogram per minute, and with normal individuals 3.13 c.c. per kilogram per minute. This increase, which is approximately but 6 per cent, is fully in line with that noted in the earlier publication, and is obviously explained in part by the fact that the metabolism of the diabetics was essentially a protein-fat metabolism, while that of the normal subjects was unquestionably a protein-fat and glycogen or carbohydrate metabolism.

As pointed out earlier, the difference between the carbon-dioxide production on these two groups of individuals does not measure by any means the difference in the actual metabolism. This is best shown by a comparison of the

[1]Benedict and Talbot, Am. Journ. Diseases of Children, 1912, 3, p. 1.

oxygen consumption. Of the 19 severe cases, the intensity of the metabolism as measured by the oxygen consumption was in each individual case higher than that of the normal individuals with whom they are compared. The single exception was Case B, the normal individual, Miss E. W., having the

TABLE 131.—*Comparison of the carbon dioxide eliminated and oxygen absorbed by diabetics and normal individuals in experiments without food.*

[Bed calorimeter and respiration apparatus.]

SEVERE DIABETES.

Diabetic.						Normal.					
Subject.	Body-weight (without clothing).	Height.	Total number of experiments.	Carbon dioxide per kilo per minute.	Oxygen per kilo per minute.	Subject.	Body-weight (without clothing).	Height.	Total number of experiments.	Carbon dioxide per kilo per minute.	Oxygen per kilo per minute.
	kilos	*cm.*		*c.c.*	*c.c.*		*kilos.*	*cm.*		*c.c.*	*c.c.*
Case A..........	51.6	171	1	3.22	4.22	A. F. G..............	53.9	175	1	3.30	3.88
	46 1	171	1	2.89	4.08	T. M. C..............	48 5	166	18	3 25	3.86
Case B..........	41 4	158	5	3.10	4.29	Miss J..............	43.3	157	3	3.30	3.74
						Miss A. C..........	42.6	165	2	3.24	3.99
						Miss E. W..........	40.5	157	2	3.78	4.57
						Mrs. S. C..........	37 4	155	2	3.26	3.77
Case C..............	62.7	166	6	2.81	4.12	H. H A..........	62.2	164	31	2.89	3.51
						S. A. R..........	61.1	165	13	2.96	3.62
	55.5	166	7	3.01	4 35	Dr P. R..........	55.2	164	9	2.89	3.55
						C. H H..........	55.1	169	9	3.14	3.72
Case D..............	48.8	173	3	3.11	4.19	T. M. C..........	48.5	166	18	3.25	3.86
Case G..............	67.1	178	1	3.22	4.38	M. A. M..........	66.0	177	54	3.12	3.68
Case H..............	52 4	159	7	3.09	4.05	Miss B..........	52.2	158	2	3 31	3.91
Case I..............	40.0	176	1	4.33	6.03	T. M. C..........	48.5	166	18	3.25	3.86
Case J..............	52.9	171	1	3.48	4.54	C. H. H..........	55.1	169	9	3.14	3.72
Case K..............	59.1	180	1	2.84	4.04	Dr. S..............	58.5	181	5	2.62	3 34
	55.6	180	3	3 31	4.65	H. F. T..............	57.8	179	44	2.86	3.32
Case L..............	63.0	183	1	3.44	4.41	E. P. C..............	63.2	185	4	2.71	3.47
	66.5	183	1	3.08	4.23	K. H. A..............	66.7	182	16	2.92	3.62
						J. R..............	66.0	182	13	3.04	3.63
Case N..............	31.5	146	7	4.11	5 57	....	.	..		....	....
Case O..............	52 6	173	3	3.06	4.24	Miss L..........	52.4	168	2	3.09	3.67
Case P..............	40.0	173	5	3.75	5.34	T. M. C..........	48.5	166	18	3.25	3 86
Case Q..............	51.7	168	2	3.36	4.37	V. G..........	54.3	162	19	3 66	4.33
						A. F. G..........	53.9	175	1	3.30	3.88
Case R..............	55.3	181	1	3.51	4.90	H. F. T..............	57.8	179	44	2.86	3.32
Case S..............	58.0	177	1	2.64	3.67	H. F. T..............	57.8	179	44	2.86	3.32
Case T..............	51.4	180	2	3 29	4.51	H. F. T..........	57.8	179	44	2.86	3.32
						A. F. G..........	53.9	175	1	3.30	3.88
Case U..............	39.5	160	5	3.80	5.20	Miss A. C..........	42.6	165	2	3.24	3.99
						Miss E. W..........	40.5	157	2	3.78	4.57
						Mrs. S. C..........	37.4	155	2	3.26	3.77
Case V............	60.0	173	1	3.42	4.72	H. B. L..............	60.0	173	7	3.19	3.84
Av. severe cases except N.......	...	..	.	**3.31**	**4.54**	Av. normal subjects.	....	...		**3.13**	**3.75**

MODERATELY SEVERE AND LIGHT DIABETES.

Case M..............	82.1	172	3	2 42	3 14	O. F. M..............	85.8	171	2	2 44	3.12
						Prof. C..........	83.0	169	3	2.40	2.88
Case W..............	59.5	161	2	2.75	3.77	Miss B. W..........	59.4	162	2	3 03	3.79
Case X..............	64.6	170	1	2.82	3.79	D. M..............	64 0	171	6	2 89	3.72
Av. moderately severe and light cases..........	...	...	..	2 66	3.57	Av. normal subjects.	. .	. .	..	2.69	3.38

higher metabolism. On the other hand, the three remaining individuals with whom Case B is compared had a much lower metabolism, the average oxygen consumption for the four normal subjects being less than that of Case B. The average oxygen consumption of the cases of severe diabetes, Case N excluded,

was 4.54 c.c. per kilogram per minute, while with the normal subjects the average oxygen consumption was 3.75 c.c. This corresponds to an increase of 0.79 c.c. per minute above normal, or somewhat over 20 per cent.[1]

In the earlier publication it was stated that the increase in metabolism was not far from 15 to 20 per cent, and it will be seen that these figures bear out perfectly this conclusion. Furthermore, taking into consideration the intimate relationship between minor muscular activity and metabolism, it is evident that these subjects should have been under exactly the same conditions in regard to the muscular activity. An examination of the many pneumograph curves obtained on these subjects shows that in these as in the earlier experiments the normal individuals were invariably somewhat more restless than were the diabetics, which would tend to increase their oxygen consumption above that of the diabetics. *If the normals had shown as little muscular activity as did the diabetics, it is obvious that their oxygen consumption would have been still less than reported, and that the increase due to the diabetes would be even greater than here shown.*

While the observations on this point have to deal more particularly with the comparison between the cases of severe diabetes and normals, it is of inter-

[1]Rolly (Deutsch. Archiv f. klin. Med., 1912, **105**, p. 494) gives the following values for his cases of severe diabetes:

Subject.	Age.	Weight.	Carbon dioxide per kilo. per minute.	Oxygen per kilo. per minute.	Respiratory quotient.
	yrs.	*kilos.*	*c.c*	*c.c.*	
H.	21	44.5	3.969	5.276	0.753
B	66	38.8	3.219	4 046	.795
Schö	21	45.3	3 791	5.168	.734
Bo.	30	40.5	3.344	4 506	.742
Schn.	34	51.5	3.565	4 892	.728
Kr.	24	61.2	3.396	4.708	.702
W. K.	20	63.5	3.281	4.830	680
U. L.	21	57.5	3.146	4.357	722
Average	..	....	3 464	4.723	...
Av. found by Benedict and Joslin for normal subjects	..	....	3.13	3.75	....

Leimdörfer (Biochem. Ztschr., 1912, **40**, p. 326) reports the nüchtern value for five severe cases as follows:

Subject.	Age.	Weight.	Height.	Carbon dioxide per kilo. per minute.	Oxygen per kilo. per minute.	Respiratory quotient.
	yrs.	*kilos.*	*cm.*	*c.c.*	*c.c.*	
Joh. Gr.	36	56.8	172	2.85	4.41	0.644
Karl Ki.	28	68	178	2.75	4.25	.645
F. S.	19	50	154	3.56	5.57	.638
Max G.	29	50	159	3.35	5.23	.641
Agn. M.	15	45	165	3.29	4.86	.678
Average	..	....	...	3 16	4 86	....
Av. found by Benedict and Joslin for normal subjects	..	....	...	3.13	3 75	....

The abnormally low quotients found by Leimdörfer with the Zuntz-Geppert method are strikingly at variance with those commonly found by us using the respiration apparatus designed in this laboratory and by Rolly using a modified form of it.

est to note that the relatively few light cases of diabetes show essentially the same carbon-dioxide production as the normal subjects, with a slightly greater oxygen consumption. This difference in oxygen consumption may easily be explained by the fact that the number of cases studied was altogether too few from which to draw deductions. If we compare the values for the severe cases of diabetes with those for the mild cases, we find that both the carbon-dioxide excretion and the oxygen consumption were materially less with the moderately severe and the light cases of diabetes than those with the severe cases. As pointed out earlier, however, they are in large part affected by the very low values found with Case M.

Comparison of the Metabolism of Diabetics with Varying Degrees of Severity.

The observations made in our earlier publication indicated that there was a tendency for the metabolism to increase *pari passu* with the severity of the diabetes, but this inference was based upon slight experimental data, the number of cases of light diabetes being very few. Similarly, in connection with the new experiments, we find a difficulty in drawing a careful deduction on this point, owing to the fact that we still have so few observations upon cases of light diabetes. A comparison of the carbon-dioxide production and oxygen consumption per kilogram of body-weight per minute, as well as the respiratory quotient, with both severe and light cases, is, however, of interest. These comparisons are given in table 132.

Table 132.—*Comparison of the metabolism of diabetics with varying degrees of severity.*

Degree of severity.	Bed calorimeter or respiration apparatus per kilogram of body-weight per minute.		All experiments with all forms of apparatus.
	Carbon dioxide eliminated.	Oxygen absorbed.	Respiratory quotient.
	c.c.	*c.c.*	
Severe cases	3.33	4.54	0.73
Moderately severe and light cases	2.82	3.73	0.75

It is obvious that with the severe cases there was a greater intensity of metabolism as indicated by an increased carbon-dioxide production and an increased oxygen consumption. On the other hand, there was a lower respiratory quotient, indicating a consumption of fat with a minimum consumption of carbohydrates; with the moderately severe and light cases there is a slightly increased respiratory quotient, corresponding to the slightly greater carbohydrate tolerance. A critical examination of these figures and the tables from which they are drawn, namely, tables 119 to 127, shows that the values for the moderately severe and light cases are enormously affected by the very low values for both carbon dioxide and oxygen found with subject M, who was distinctly fat. While, therefore, the original contention may be made that in severe diabetes a somewhat higher metabolism is shown than in moderately severe or

light cases, nevertheless there is a serious objection to this form of comparison owing to the fact that we have so few light cases. If, however, we examine the figures in table 120, we see that if Case M be omitted the carbon-dioxide production is still lower with the two remaining cases than the average value for the severe cases. Similarly, if the low oxygen consumption of Case M be omitted in table 123, the average oxygen consumption with severe cases is greater than with any of the moderately severe cases; hence it seems perfectly justifiable to state that the more severe the case, the greater the intensity of the metabolism. Thus the experimental evidence seems to justify fully our earlier contention to this effect.

A Comparison of the Metabolism of Fasting Diabetics under Varying Conditions as to the Intensity of the Acidosis.

As was pointed out in the earlier report, there was a period in the history of Case A when he was apparently in a much more serious condition than at any other time. During this period the evidence was clear that both his metabolism and pulse-rate were considerably higher than at other times. This suggested a relationship between metabolism and the degree of severity of the diabetes, a suggestion that was emphasized and accentuated by the fact that the whole group of subjects with severe diabetes indicated a higher metabolism than did those with light diabetes, although admittedly the number of the latter was too few for us to draw any definite deductions.

In the new cases here reported at least two gave indications of a markedly different severity of the disease within a very short period of time, and these fluctuations in severity occurred during the experimental period at the laboratory. Both cases were boys. With Case N it was noted that on days following green days the metabolism was high, there was a higher excretion of β-oxybutyric acid, the pulse-rate was high and the alveolar carbon-dioxide tension was low. On days following oatmeal days, on the other hand, the metabolism was distinctly lower, the pulse-rate lower, and the alveolar carbon-dioxide tension was higher. The results with this case were, however, complicated by an uncertainty as to whether there was not a surreptitious ingestion of food; since the ingestion of food *per se* would stimulate metabolism, it is uncertain whether the high metabolism experienced on certain dates was due to the severity of the disease or to the previous ingestion of food. Nevertheless the other evidence, particularly the carbohydrate balance, is of material assistance in determining whether or no food was ingested prior to coming to the laboratory, and we believe that for the two days here cited there is reasonable ground for belief that the actual conditions of metabolism were not complicated by the previous ingestion of food. The results are given in table 133.

On November 30 to December 1 the acidosis was severe; the β-oxybutyric acid, which was fortunately determined on that day, amounted to 35 grams, with a minus carbohydrate balance of 25 grams; the oxygen consumption was 179 c.c. with a pulse-rate of 75 and a carbon-dioxide tension of 17 mm. On December 1 the subject had an oatmeal day, and on December 2 to 3, the dia-

cetic acid reaction and the carbohydrate balance were essentially the same, but there was a fall in the ammonia-nitrogen nitrogen ratio; there was, however, a considerably lower metabolism, inasmuch as but 160 c.c. of oxygen were consumed per minute, the pulse-rate was 57, and the alveolar carbon-dioxide tension was 26 mm. Unfortunately the β-oxybutyric acid was not determined.

In examining the original table for this case (table 33) we find varying days, even when the subject was supposed to be fasting, the variations in the oxygen consumption ranging from 179 down to as low as 160. These high days can not always be sharply designated as being days on which no food was taken, as we have reason to believe that the subject took food on one or two occasions before coming to the laboratory, either through a misunderstanding or otherwise, and it was not properly reported. In any event, the relationship between the intensity of the metabolism, the diet of the previous day, and the general physical condition of the subject was such as to be of considerable significance, and seemed to indicate a rather close connection between the severity of the acidosis and the intensity of metabolism.

TABLE 133.—*Comparison of the metabolism of Case N under varying conditions of acidosis.*

Date.	Diacetic acid.	β-oxy-butyric acid.	$\frac{NH^3-N}{Total\ N}$.	Carbo-hydrate balance.	Metabolism at beginning of following day.		Alveolar carbon-dioxide tension.
					Oxygen per kilogram per minute.	Pulse-rate.	
1910.		*gms.*	*p. ct.*	*gms.*	*c.c.*		*mm.*
Nov. 30–Dec. 1..........	++++	35	42	−25	179	75	17
Dec. 2–3................	++++	?	36	−15	160	57	26

With Case Q we are confident that the diet was properly controlled. We have accordingly selected two days with this subject in which both the degree of acidosis and the total metabolism were determined. The results are given in table 134. Under these conditions we find on November 18–19, when there was severe acidosis with a large amount of β-oxybutyric acid and a low carbohydrate balance, that the metabolism and pulse-rate were considerably higher than three days later, when the β-oxybutyric acid was two-thirds that of the first and the positive carbohydrate balance was considerable, this day being a carbohydrate oatmeal day. There was likewise an increase in the tension of the alveolar carbon dioxide. On the other hand, the whole comparison is somewhat complicated by the fact that the volume of urine on the second day was but one-half that of the first day; the total amount of nitrogen was also lower. This of course would keep up the high percentage of ammonia nitrogen, and might account for the low excretion of β-oxybutyric acid, but need not necessarily affect the carbohydrate balance. It is much to be regretted that other experiments without food could not have been made with this subject, but the only other two experiments obtained with him were after definite feeding.

The results of the experiments with Cases N and Q strongly suggest an intimate relationship between the severity of diabetes and high metabolism;

while this evidence from experiments with individual subjects is by no means conclusive, it supplements the general impression derived from experiments with different individuals that with severe diabetes there is a high metabolism, and with mild diabetes a lower metabolism. This last inference, however, is drawn from experiments with different individuals, while the experiments with Cases N and Q imply that with the same individual, differences in intensity of the disease may be accompanied by differences in the intensity of the metabolism as measured by the oxygen consumption, the pulse-rate, and the alteration in the carbon-dioxide tension of the alveolar air.

TABLE 134.—*Comparison of the metabolism of Case Q under varying conditions of acidosis.*

Date.	Diacetic acid.	β-oxy-butyric acid.	$\frac{NH_3-N}{Total\ N}$.	Carbo-hydrate balance.	Metabolism at beginning of following day.		Alveolar carbon-dioxide tension.
					Oxygen per kilo-gram per minute.	Pulse-rate.	
1910.		*gms.*	*p. ct.*	*gms.*	*c.c.*		*mm.*
Nov. 18-19	+++	30	27.4	−55	232	79	31
Nov. 22-23	++++	19.6	25.9	+75	220	65	40

THE INFLUENCE OF A NORMALLY INDUCED ACIDOSIS UPON METABOLISM.

Since diabetics with severe acidosis showed a higher metabolism than did light cases, and since the metabolism was higher with the same individual when the diabetes was very severe than when it was milder, it seemed desirable to find out the effect of an experimentally induced acidosis upon the metabolism of normal individuals. While studying in the laboratory of Dr. Joseph Barcroft, of Cambridge, England, Mr. H. L. Higgins, an associate in this laboratory, made some interesting observations on the relationship between the effect of a carbohydrate-free diet and the dissociation curve of the blood. While upon a carbohydrate-free diet he observed great lassitude and a general feeling of malaise. On repeating this experiment in the fall of 1911, it occurred to him that a study of the metabolism as measured by the oxygen consumption and carbon-dioxide production during this period would be of interest, and hence some observations were made of the total metabolism. Subsequently, a second experiment was made with another subject, H. H. A., a student in the Harvard Medical School. This was more carefully planned, with the special purpose of studying the effect of the carbohydrate-free diet upon the metabolism.

In a paper recently published by Benedict and Higgins,[1] discussing the effect of the amount of carbohydrates in the preceding diet upon the respiratory quotient, it was shown that the respiratory quotient with a carbohydrate-free diet was as low as the ordinary quotients in diabetes, if not lower, and that the respiratory quotient could be elevated persistently by increasing the quan-

[1]Benedict and Higgins, Am. Journ. Physiol., 1912, 30, p. 217.

tity of carbohydrates in the diet. Inasmuch as this paper dealt especially with the character and not with the amount of the metabolism, practically no reference was made to the significant fact that apparently the lower the amount of carbohydrates in the diet, the higher the metabolism. It is the purpose of the following section of this discussion to state the details of these experiments and to discuss the results.

EXPERIMENTS WITH H. L. H.

The study made with this subject included four experiments, all with the respiration apparatus. Three of these were made with the carbohydrate-free diet; the fourth followed normal diet. The special diet was begun on September 6, 1911, but the plan to study the respiratory exchange was not developed until the next day, so that the first respiration experiment was made on September 7, 1911. The experiment on normal diet was therefore delayed until the second day after the discontinuance of the carbohydrate-free diet. The vital statistics for this subject are as follows:

Date of birth, March 26, 1887; height, 172 centimeters; body-weight without clothing during experiments, 60.2 kilos.

STATISTICS OF EXPERIMENTS WITH H. L. H.

Respiration Experiment No. 1.

Date, September 7, 1911. Body-weight without clothing, 60.2 kilos.

The last meal preceding the beginning of the carbohydrate-free diet was taken at 12^h 30^m p. m., September 5, and consisted of beef stew with vegetables and bread and butter. The subject fasted the remainder of the day. On the day preceding the first experiment he took for his breakfast eggs and beef tea; for dinner, sardines and cheese; and for supper, pork chops. Samples of the alveolar air were taken at 2^h 56^m and 3^h 52^m p. m. on this day.

On the experimental day the subject came to the laboratory fasting; the experiment began at 8^h 50^m a. m., continued for three 15-minute periods, with intermissions of 19 and 11 minutes respectively, and ended at 9^h 55^m a. m. The pulse-rate ranged from 80 to 88. The results of the experiment are given in table 135. After the experiment was over the subject ate for his breakfast at 10 a. m. soft-boiled eggs with butter; also took pepsin gum. For his dinner, at 3^h 30^m p. m., he again took soft-boiled eggs with butter, while for his supper he ate fried ham with a little butter.

Respiration Experiment No. 2

Date, September 8, 1911. Body-weight without clothing, 60.2 kilos. (assumed).

At 8 a. m. on the experimental day the subject took a few sips of coffee, a piece of pepsin gum, and a little lemon juice. The experiment began at 9^h 25^m a. m., continued for three 15-minute periods with intermissions of 11 and 9 minutes each, and ended at 10^h 30^m a. m. The pulse-rate ranged from 72 to 80. The food taken by the subject throughout the day consisted of a breakfast of lamb chops at 10^h 30^m a. m., a dinner of sardines at 2^h 30^m p. m., and a supper of beefsteak at 8 p. m.. Samples of the alveolar air were taken on this day. The results of the experiment are given in table 135.

Respiration Experiment No. 3.

Date, September 9, 1911. Body-weight without clothing, 60.2 kilos. (assumed).

This experiment began at 9^h 53^m a. m. with the subject fasting, was continued for two 15-minute periods, and ended at 10^h 31^m a. m. The pulse-rate ranged from 64 to 78. The carbohydrate-free diet was discontinued beginning with this day, no record being made of the food eaten on this and succeeding days. The results of the experiment may be found in table 135.

Respiration Experiment No. 4.

Date, September 11, 1911. Body-weight without clothing, 60.2 kilos. (assumed).

On the second day after the discontinuance of the carbohydrate-free diet, another respiration experiment was made with the subject after a 12-hour fast. The experiment began at 8^h 22^m a. m., continued for three 15-minute periods, and ended at 9^h 37^m a. m. The pulse-rate ranged from 66 to 72. The results of the experiment are given in table 135.

Table 135.—*Results of respiration experiments Nos. 1 to 4 with H. L. H., without food.*

Experiment No.	Date.	Diet and time.	Duration.	Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration-rate.
	1911.	*Carbohydrate free.*[1]	*min. sec.*	*c.c.*	*c.c.*			
1	Sept. 7..	8^h 50^m a.m......	15 4	206	305	0.68	85	16
		9 14 a.m......	15 7	197	292	.67	83	15
		9 40 a.m......	15 10	198	301	.66	84	16
		Average.......	..	**200**	**299**	**.67**	**84**	**16**
2	Sept. 8..	9^h 25^m a.m......	15 7	209	281	.75	76	16
		9 51 a.m.	15 4	196	279	.70	75	17
		10 15 a.m.. ...	15 6	189	280	.68	74	16
		Average... ...	..	**198**	**280**	**.71**	**75**	**16**
3	Sept. 9..	9^h 53^m a.m......	15 9	198	276	.72	70	16
		10 16 a.m......	15 4	191	268	.71	74	16
		Average.......	..	**195**	**272**	**.72**	**72**	**16**
		Normal.[2]						
4	Sept. 11.	8^h 22^m a.m. ...	15 24	212	248	.86	69	16
		8 50 a.m.. .	15 40	207	233	.89	67	17
		9 21 a.m. .	15 18	211	248	.85	71	15
		Average..... .	..	**210**	**243**	**.87**	**69**	**16**

[1] Subject began the carbohydrate-free diet after the noon meal of Sept. 5, 1911.
[2] Subject resumed his normal diet on the morning of Sept. 9, 1911.

RESULTS OF EXPERIMENTS WITH H. L. H.

It is obvious from the data given in table 135 for the oxygen consumption that the metabolism was much higher during the carbohydrate-free diet than during the normal diet. This is further substantiated by the fact that the pulse-rate was higher, particularly on the first day on which measurements were secured.

Table 136.—*Statistics of urine—Subject H. L. H.*

Date.	Period.	Volume of urine.	Acetone.	β-oxy-butyric acid.	Nitrogen.	Ammonia. Total.	Ammonia. $\frac{NH_3-N}{\text{Total N}}$.
1911.		*c.c.*	*gms.*	*gms.*	*gms.*	*gms.*	*p. ct.*
Sept. 6–7[1]..	8^h 45^m a.m. to 8^h 25^m a.m............	1130	1.548	4.247	21 92	1.58	5.9
7–8...	8 25 a.m. 7 50 a.m	1120	1.726	.....	18.05	2.46	11.2
8–9...	7 50 a.m. 9 35 a.m............	1300	2.792	8.028	18.93	4.07	17.7

[1] The subject subsisted on a carbohydrate-free diet after the noon meal of Sept. 5, 1911.

Urine analyses.—To study the degree of acidosis, the subject made a careful urine analysis on three days of the study. The results of these analyses are reported in table 136. Unfortunately, the value for β-oxybutyric acid on September 7–8 is questionable and is therefore not included. It will be seen that there was a measurable amount of acetone and β-oxybutyric acid appearing in the urine; there was also an increase in the amount of ammonia which rose on the last day to about 4 grams with approximately 18 per cent of the total nitrogen in the form of ammonia-nitrogen. These commonly accepted indices of an acidosis are particularly well shown in this experiment.

Composition of the alveolar air.—This subject had been particularly interested in studying the composition of alveolar air and so made a number of observations upon himself prior to and during the experiment, the results of which are given in table 137. Of special interest is the carbon-dioxide tension, which falls below the normal immediately after the beginning of the carbohydrate-free diet, the average on September 8 being some 7 mm. below the normal. The oxygen consumption shows a corresponding increase.

TABLE 137.—*Determinations made on alveolar air with H. L. H.*

Date and time.	Carbon-dioxide tension.	Oxygen tension.	Diet.
1911.	*mm.*	*mm.*	
July 21–22, average..	36.5	111.1	Normal.
Sept. 6:			
$2^h\ 56^m$ p.m........	35.5	103.8	Carbohydrate-free.[1]
3 52 p.m........	33.9		
Sept. 8[2]........	29.9	120.4	Carbohydrate-free.
	28.6		
	30.3		
Average.........	29.6	120.4	

[1] Subject began the carbohydrate-free diet after the noon meal of Sept. 5, 1911. He ate food at $12^h\ 20^m$ p.m. Sept. 6.
[2] Probably after food.

EXPERIMENTS WITH H. H. A.

The important point observed in connection with the study with H. L. H., namely, an increased metabolism incidental to the ingestion of a carbohydrate-free diet, justified a second carefully-planned study on another subject. The subject of this second study was placed in the New England Deaconess Hospital, so that the diet was under rigid control throughout the entire period. Being a medical student and a man of unusual intellectual keenness in the problems involved, he cooperated most heartily with us in all these tests.

A series of nine experiments was made with this subject, including a preliminary experiment with a normal diet, five experiments with a carbohydrate-free diet, one experiment during which oatmeal was ingested, one experiment with cane sugar, and a final experiment following a normal diet. The vital statistics of the subject were as follows:

Date of birth, August 10, 1890; height, 164 cm.; range in body-weight during experiments, 60.9 to 63.5 kilos.

STATISTICS OF EXPERIMENTS WITH H. H. A.

Respiration Experiment No. 1.

Date, December 27, 1911. Body-weight without clothing, 63.5 kilos.

The diet on the day preceding the study was a mixed diet. Breakfast: coffee, with sugar, fried potatoes, and bread. Dinner: barley soup, potatoes, bread, apple pie, coffee, hard candy. Supper: fried potatoes, tea with sugar, bread, and a few dates.

On the experimental day the subject came to the laboratory without breakfast and lay down upon the couch at 8 a. m. The experiment began at $8^h\ 50^m$ a. m., continued for four 15-minute periods with intervals of 8 to 10 minutes, and ended at $10^h\ 18^m$ a. m. The pulse-rate ranged from 74 to 82. The subject urinated before the experiment at 7 a. m., and after it was over, at $10^h\ 25^m$ a. m. A sample of the blood was taken at $11^h\ 10^m$ a. m. The results of the experiment may be found in table 138.

Respiration Experiment No. 2.

Date, December 27, 1911. Body-weight without clothing, 63.5 kilos.

This experiment was made on the afternoon of the day of the preceding experiment, being the first with a carbohydrate-free diet. At 12 o'clock noon the subject took for his dinner steak and butter, with a cupful of beef tea. The experiment, which consisted of two 15-minute periods, began at $4^h\ 38^m$ p. m. and ended at $5^h\ 19^m$ p. m. The pulse-rate ranged from 94 to 104. After the experiment the subject ate for his supper, at 6 p.m., scrambled eggs, butter, and tea without milk or sugar. The results of the experiment are given in table 138.

Respiration Experiment No. 3.

Date, December 28, 1911. Weight without clothing, 61.9 kilos.

The subject came to the laboratory without breakfast, lay down upon the couch at $7^h\ 45^m$ a. m., and a blood sample was taken about $8^h\ 12^m$ a. m. The experiment began at 9 a. m., continued for three 16-minute periods, and ended at $10^h\ 03^m$ a. m. The pulse-rate ranged from 78 to 88. The subject urinated at $10^h\ 35^m$ a. m.

The diet for this day consisted of eggs, butter, and coffee at 12 o'clock; cheese, fried eggs, bacon, and beef tea at 3 p. m., and lean pork chops and tea at $7^h\ 30^m$ p. m. The results of the experiment may be found in table 138.

Respiration Experiment No. 4.

Date, December 29, 1911. Body-weight without clothing, 61.3 kilos.

Previous to the experiment, the subject said he felt very well, fully equal to taking a long walk. He came to the laboratory without breakfast. The experiment began at $8^h\ 12^m$ a. m. and continued for five periods of 15 to 16 minutes each. The subject urinated at 7 and $11^h\ 25^m$ a. m. On this day he ate, at $12^h\ 35^m$ p. m., eggs and fried ham, with weak coffee; at 3 p. m., boiled scrod with butter, and beef tea; and at 7 p. m., fried lamb chops and tea. The results of the experiment are given in table 138.

Respiration Experiment No. 5.

Date, December 30, 1911. Body-weight without clothing, 61 kilos.

No breakfast was taken by the subject on the day of the experiment. The respiration experiment began at $10^h\ 46^m$ a. m. and continued for one 8-minute and two 15-minute periods, ending at $12^h\ 12^m$ p. m. The pulse-rate during the experiment ranged from 67 to 78. The subject urinated at 7 a. m. and $12^h\ 30^m$ p. m. He took food during the day as follows: $1^h\ 10^m$ p. m., scrambled eggs,

butter, cheese, and beef tea; 3^h 30^m p.m., beefsteak and butter; 7^h 30^m p. m., boiled chicken, butter, and eggs. The results of the experiment are included in table 138.

Respiration Experiment No. 6.

Date, December 31, 1911. Body-weight without clothing, 61 kilos.

As usual, the subject fasted for 12 or more hours previous to the experiment. He lay down upon the couch at 8^h 04^m a. m., the experiment beginning at 9^h 01^m a. m. The measurements were made in three 15-minute periods, ending at 10^h 30^m a. m. The pulse-rate during the experiment ranged from 75 to 83.

During the day the subject ate as follows: At 1 p. m., boiled eggs, including a little of the whites, butter, and cream (32 per cent fat) with soda; at 3^h 30^m p. m., eggs (yolks only), bacon, and beef tea; at 7^h 30^m p. m., eggs (yolks), olive oil, cream with soda, and tea. He said subsequently that he felt very thirsty on this day, and drank considerable water, but this did not affect the volume of the urine. Table 138 gives the results of the experiment.

Respiration Experiment No. 7.

Date, January 1, 1912. Body-weight without clothing, 60.9 kilos.

The experiment was divided into two sections with an interval of some 3 hours; in the first part the subject fasted for three periods; shortly before the second part of the experiment began he ate a considerable amount of oatmeal and eight periods followed, an additional portion of oatmeal being taken before the last two periods.

The subject lay down upon the couch at 7^h 45^m a. m., and the experiment began at 8^h 22^m a. m. The fasting periods ended at 9^h 51^m a. m. At 12^h 12^m p. m., the subject took 582.8 grams of cooked oatmeal, 83.6 grams of butter, and 400 c.c. of water. The following six 15-minute periods began at 12^h 41^m p. m. and ended at 4^h 18^m p. m. At 4^h 35^m p. m. the subject ate a second portion of oatmeal (350.7 grams) and butter (65.1 grams) and drank 400 c.c. of water. The two last periods of the experiment began at 5^h 23^m p. m., and ended at 6 p. m. In the first period after food, the subject probably went to sleep for a moment or so. In the final period he coughed during the last minute of the experiment. The times of urinating were 7 a. m., 10^h 15^m a. m., 11^h 55^m a. m., 3^h 05^m p. m., and 6^h 15^m p. m. The pulse-rate during the fasting periods ranged from 76 to 84, while during the periods following the ingestion of food it ranged from 75 to 93. The measurements of the metabolism are given in table 138.

Respiration Experiment No. 8.

Date, January 2, 1912. Body-weight without clothing, 61.2 kilos.

This experiment was divided into two sections, the first three periods being fasting, and the last six periods following the ingestion of cane sugar. For supper the night preceding the experiment the subject took coffee with sugar, and bread.

The fasting periods began at 7^h 42^m a. m. and ended at 8^h 45^m a. m. At 9^h 12^m a. m., the subject took 100 grams of cane sugar in 400 c.c. of water and lemon juice. The following periods began at 9^h 22^m a. m., ending at 12^h 57^m p. m. During the fasting periods the pulse-rate ranged from 64 to 68; in the periods following the taking of the cane sugar it ranged from 73 to 86. The subject urinated at 10^h 30^m a. m., also urinated and defecated between the eighth and ninth periods, resting afterwards for about 15 minutes. The results of the experiment are to be found in table 138.

Respiration Experiment No. 9.

Date, January 3, 1912. Body-weight without clothing, 62.5 kilos.

After leaving the laboratory at 1 p. m., January 2, the subject drank, at 1^h30^m p. m., two cupfuls of coffee with sugar and ate an egg sandwich. At 6 p. m. he took beef stew with potatoes, bread, coffee, rice pudding, and apple pie.

Table 138.—*Results of respiration experiments Nos. 1 to 9 with H. H. A.*

Experiment No.	Date.	Diet and time.	Duration.	Carbon dioxide eliminated per minute.	Oxygen absorbed per minute.	Respiratory quotient.	Average pulse-rate.	Average respiration-rate.
		Normal.						
	1911.	Without food:	*min. sec.*	*c.c.*	*c.c.*			
1	Dec. 27..	$8^h 50^m$ a.m....	14 23	208	225	0.93	76	12
		9 13 a.m....	14 19	208	223	.93	77	11
		9 37 a.m....	14 16	193	228	.85	78	12
		10 02 a.m....	15 30	195	221	.88	79	13
		Average.. ...	..	**201**	**224**	**.90**	**78**	**12**
		Carbohydrate-free.						
		With food:[1]						
2	Dec. 27..	$4^h 38^m$ p.m....	14 54	205	289	.71	98	14
		5 04 p.m....	14 46	209	290	.72	102	12
		Without food:						
3	Dec. 28..	$9^h 00^m$ a.m....	15 55	189	263	.72	83	11
		9 22 a.m....	15 52	187	250	.75	81	14
		9 47 a.m....	15 51	195	262	.74	84	12
		Average......	.. ..	**190**	**258**	**.74**	**83**	**12**
4	Dec. 29..	$8^h 12^m$ a.m....	15 28	176	262	.67	73	12
		8 38 a.m....	15 52	176	273	.65	74	11
		9 05 a.m....	15 48	177	247	.72	73	10
		9 59 a.m....	15 37	183	264	.69	74	10
		10 48 a.m....	15 05	184	246	.75	74	12
		Average......	.. ..	**179**	**258**	**.70**	**74**	**11**
5	Dec. 30..	$10^h 46^m$ a.m....	7 44	185	250	.74	69	11
		11 03 a.m....	14 58	171	237	.72	70	10
		11 57 a.m....	15 05	177	235	.75	72	9
		Average......	.. ..	**178**	**241**	**.74**	**70**	**10**
6	Dec. 31..	$9^h 01^m$ a.m....	14 35	169	242	.70	79	14
		9 35 a.m....	14 39	175	238	.73	80	14
		10 16 a.m....	14 22	175	246	.71	77	13
		Average.....	.. ..	**173**	**242**	**.71**	**79**	**14**
7	1912. Jan. 1....	$8^h 22^m$ a.m....	14 40	162	240	.67	81	14
		9 07 a.m....	14 49	160	233	69	77	14
		9 36 a.m....	15 05	169	243	.70	79	13
		Average....	..	**164**	**239**	**.69**	**79**	**14**
		Oatmeal and butter.						
		With food:						
		$12^h 41^m$ p.m.[2]..	14 52	180	267	.67	84	16
		1 08 p.m....	15 07	192	275	.70	86	16
		1 41 p.m....	15 12	199	275	.72	82	15
		2 08 p.m....	15 39	204	274	.74	92	16
		3 33 p.m....	15 13	207	283	.73	85	11
		4 04 p.m....	14 12	186	254	.73	77	13
		5 23 p.m.[3]..	15 02	208	284	.73	82	13
		5 45 p.m....	14 42	211	291	.72	84	14
		Without food:						
8	Jan. 2....	$7^h 42^m$ a.m....	14 27	158	223	.71	67	11
		8 05 a.m....	15 16	146	208	.70	65	13
		8 29 a.m....	15 41	156	215	.73	67	11
		Average......	..	**153**	**216**	**.71**	**66**	**12**
		Cane sugar.						
		With food:[4]						
		$9^h 22^m$ a.m....	14 01	209	241	.87	73	11
		9 45 a.m....	14 09	242	232	1.04	79	15
		10 14 a.m....	14 28	238	245	.97	76	15
		11 05 a.m....	15 08	229	247	.93	80	15
		11 34 a.m....	14 32	201	241	.83	85	14
		12 41 p.m....	14 30	173	230	.75	80	12
		Normal.						
		Without food:						
9	Jan. 3....	$7^h 55^m$ a.m....	16 04	172	216	.79	74	10
		8 24 a.m....	15 05	169	212	.80	73	8
		Average......	..	**171**	**214**	**.80**	**74**	**9**

[1] Subject ate 169 gms. beefsteak, 14.5 gms. butter, and 1 cup beef tea at 12 noon.
[2] Subject ate 582.8 gms. cooked oatmeal and 83.6 gms. butter at $12^h 12^m$ p.m.
[3] Subject ate 350.7 gms. cooked oatmeal and 65.1 gms. butter at $4^h 35^m$ p.m.
[4] Subject took 100 gms. cane sugar in 400 c.c. of water with juice of lemon at $9^h 12^m$ a.m.

On the experimental day the subject came to the laboratory fasting, and the experiment began at 7^{h} 55^{m} a. m., continuing for two periods of approximately 15 minutes each and ending at 8^{h} 39^{m} a. m. During the experiment the pulse-rate ranged from 72 to 75. The measurements of the metabolism are given in table 138.

RESULTS OF EXPERIMENTS WITH H. H. A.

The measurements of the total metabolism of the subject for the whole series of experiments are given in table 138. Previous to the first experiment the subject had been on a normal diet, but fasted for some 12 hours before coming to the laboratory. Under these conditions he absorbed about 225 c.c. of oxygen per minute and had an average pulse-rate of approximately 78. On the morning following the carbohydrate-free diet, the oxygen absorption was increased to approximately 255 c.c. per minute, and the pulse-rate to 83. On the next four days of the carbohydrate-free diet, the metabolism remained high, although there was a tendency for it to approximate more nearly the normal level as the experiment progressed. Singularly enough, notwithstanding the high metabolism, the pulse-rate on the first two days was considerably below that on the normal day. Unfortunately simultaneous observations with regard to the blood-pressure were not obtained.

TABLE 139.—*Statistics of urine*[1]—*Subject H. H. A.*

Date.	Volume of urine.	Specific gravity.	Color.	Reaction.	Diacetic acid.	β-oxybutyric acid.	Nitrogen.	Ammonia. Total	Ammonia. $\frac{NH_3-N}{Total\ N}$	Salt.	Alkali retention by kidneys, c.c. N/10 NaOH	Diet.
1911.	*c.c.*					*gms.*	*gms.*	*gms.*	*p.ct.*	*gms.*		
Dec. 25–26.	1245	1 0155	Pale..	Acid	..	....	10.22	0.88	7.1	11.6	174.3	Normal.
Dec. 26–27.	1974	1 013	Slightly pale.	Acid	..	...	9.39	.87	7.6	20.9	197.4	Do.
Dec. 27–28.	1667	1 018	Normal ...	Acid	...	.. .	11.82	.56	3.9	14.0	100.0	Carbohydrate-free
Dec. 28–29.	985	1 0285	Normal .	Acid	0	....	16.45	1.0	5.0	8.6	384.1	Do.
Dec. 29–30	1304	1 026	Pale	Acid	0	....	21.28	1.27	4.9	6.3	326.0	Do.
Dec. 30–31	928	1.0265	Normal . ..	Acid	..	.....	17.52	1.62	7.6	7.1	352.6	Do.
Dec. 31–Jan. 1 ..	880	1 026	Normal.....	Acid.	0	4.8	14.63	1.93	10.9	5.8	423.6	Do.
1912.												
Jan. 1– 2	991	1 016	Pale.........	Acid.	0	...	8 72	1.75	16.5	......	297.0	Oatmeal.[2]
Jan. 2– 3	818	1.0165	Pale.........	Acid.	0	....	6 62	1.29	16.0	......	237.2	Cane sugar.[3]
Jan. 3– 4	648	1.023	....	......	..	....	7.18	....	......	......	194.4	Normal.

[1]Sugar and albumen tested for each day and uniformly absent.
[2]Subject ate 582.8 gms. cooked oatmeal and 83.6 gms. butter at 12.12 p.m.; also 350.7 gms. cooked oatmeal and 65.1 gms. butter at 4.35 p.m. See statistics of experiment No. 7.
[3]Subject took 100 gms. cane sugar in 400 c.c. of water with juice of lemon at 9.12 a.m. For diet rest of day see statistics of experiments Nos. 8 and 9.

Urine analyses.—The urine was collected in 24-hour periods from December 25 to January 4, although on certain days the determinations were made in periods corresponding to the experimental periods. The results of the urine analyses are given in table 139. Only one determination of the β-oxybutyric acid was made, *i. e.*, on the fifth day of the carbohydrate-free diet, and 4.8 grams of β-oxybutyric acid were found. There was no diacetic-acid reaction, but the percentage of ammonia-nitrogen to total nitrogen was somewhat higher than normal, if not excessively high. On the oatmeal and cane-sugar days following the carbohydrate-free diet, the percentage of ammonia-nitrogen in

the proportion of total nitrogen increased considerably, this being largely due to the fact that there was a decided decrease in the total nitrogen. Sugar and albumen were tested for each day and were uniformly absent.

The general picture of the urine analyses with this subject does not by any means indicate as striking an acidosis as was found with subject H. L. H. On the other hand, it is reasonably clear from the presence of β-oxybutyric acid that there was an acidosis, and that this was due to the carbohydrate-free diet. The absence of the determinations of β-oxybutyric acid on the other days is much to be regretted.

The alkali retention by the kidney, which, taken together with the ammonia excretion, makes up the protective mechanism of the body against acidosis, shows an increase during the days of carbohydrate-free diet and a return toward normal with the addition of carbohydrates to the food, following closely the ammonia curve.[1]

TABLE 140.—*Determinations made on alveolar air with H. H. A.*

Date.	Carbon dioxide.		Remarks.	Date.	Carbon dioxide.		Remarks.
	Per cent.	Tension.			Per cent.	Tension.	
1911.		*mm.*		1911.		*mm.*	
Dec. 26..	5.62	. .	At about 3 p.m.; probably food taken about noon.	Dec. 31.	4.70	....	About 11 p.m.; before eating.
	5.43	.			4.64	....	
	5.46				4.53	....	
	5.68	.			4.69	....	
	5.94	.		Av..	4.64	33.2	
	5.60	. .		1912. Jan. 1	4.34	....	About 10 a.m.; before eating.
Av	5.62	40.1			4.53	. . .	
Dec. 28.	5.11	. .	About 10^h45^m a.m.; before eating		4.39		
	5.04	.			4.75		
	5.00	.			4.56	.	
Av...	5.05	35.6			4.76		
Dec. 29.	4.81	.	About 11^h45^m a.m.; before eating.		4.70		
	4.67	.		Av.	4.58	32.6	
	4.66			Jan. 1.	5.27	. . .	At 2^h 30^m p.m.; after oatmeal and butter at 12^h 12^m p.m.
	4.85	.			5.18	.	
Av...	4.75	33.9		Av.	5.23	37.2	
Dec. 30...	4.54	.	About 12^h15^m p.m.; before eating.	Jan. 1.	5.10		At 6^h 15^m p.m. after oatmeal and butter at 4^h 35^m p.m.
	4.85	.			5.02	. .	
	4.79				5.03	. . .	
	4.87	. . .					
Av....	4.76	34.4		Av...	5.05	36.0	

Composition of the alveolar air.—Determinations of the alveolar air, with particular reference to the carbon-dioxide percentage and tension, were made on a number of days throughout this test. The results are presented in table 140. The normal value found when the subject began the carbohydrate-free diet was 5.62 per cent of carbon dioxide, corresponding to about 40.1 mm. tension. With the carbohydrate-free diet this tension dropped almost immediately, and reached its minimum on the fifth day, 32.6 mm. On the resumption of a normal diet with oatmeal there was an immediate response and an increase

[1] H. M. Adler and G. Blake, Archives of Internal Medicine, 1911, 7, p. 479.

in the carbon-dioxide tension to 37.2 mm. The correlation, therefore, between the carbon-dioxide tension, the alveolar air, the total metabolism and the acidosis is clearly shown.

Blood examination.—The blood was examined daily and the results are reported in table 141.

TABLE 141.—*Results of blood examinations*[1]—*Subject H. H. A.*

Date and time.	Time after last meal.	Hemoglobin (Fleischl).	White blood-corpuscles.	Red blood-corpuscles.
Dec. 27, 1911:	*hrs. min.*	*p. ct.*		
$4^h\ 00^m$ p.m.	4 0	95	17,300	5,860,000
Dec. 28, 1911:				
$8^h\ 12^m$ a.m.	14 0	..	10,600	....
4 00 p.m.	1 0	96	11,100	5,676,000
Dec. 29, 1911:				
$4^h\ 00^m$ p.m.	1 0	95	11,700	5,864,000
Dec. 30, 1911:				
$4^h\ 00^m$ p.m.	30	96	8,000	6,128,000

[1] On Dec. 28 a stained specimen of the blood was examined microscopically with the following result: Differential count of 200 white blood-corpuscles showed polynuclear leucocytes 82.5 per cent, lymphocytes 15.5 per cent, transitionals 1 per cent, eosinophiles 1 per cent. The red blood-corpuscles showed nothing abnormal.

It will be seen that the hemoglobin was constant for the four days; the number of red blood-corpuscles was also essentially constant. We are unable to explain the increase in the number of white blood-corpuscles on the first afternoon after the first carbohydrate-free meal. The slight decrease in the white blood-corpuscles found for the following successive days does not warrant conclusions, particularly without support from similar experiments.

The differential count of the white blood-corpuscles shows nothing abnormal.

RELATIONS BETWEEN A NORMALLY INDUCED ACIDOSIS AND THE OBSERVED INCREASE IN THE METABOLISM IN SEVERE DIABETES.

With both of these subjects there was a noticeable increase in the total metabolism as measured by the oxygen consumption, coincident with the use of a carbohydrate-free diet. With one case at least there was a corresponding increase in the pulse-rate, while with the other there was a temporary increase in the pulse-rate, followed by a decline. Since it is probable that an intimate relationship exists between the blood-pressure and the pulse-rate, we have every reason to believe that if all the data had been available this seeming discrepancy between the results with the two subjects could be readily explained.

If the presence of the small amount of β-oxybutyric acid found with these subjects was sufficient to stimulate the metabolism so that the metabolic activity of the body itself as a whole was increased by the amount here found, it is not at all surprising that in severe diabetes the same processes which involved the formation and circulation of β-oxybutyric acid molecules would likewise tend to stimulate the body activity of the diabetic. On the other hand, the constant presence of β-oxybutyric acid throughout a long period of time during the course of the disease might easily lead to an acquired tolerance for the presence of β-oxybutyric acid which would involve the necessity for the

presence of a very much larger amount of the acid in order to produce a given stimulating effect.

In a recently concluded experiment with a fasting man in this laboratory, after 31 days of fasting it was found that the amount of β-oxybutyric acid in the urine was not materially greater than that found with these two subjects when they were subsisting upon a carbohydrate-free diet. There was, however, no measurable increase in the metabolism noted with this subject; on the contrary there was a marked decline in total metabolism as the fast progressed. While, therefore, it would appear possible to explain the increased metabolism noted with diabetics upon the ground that the severity of the acidosis caused an increased metabolism, we can at present only state the fact that coincidental with the severe acidosis there was found an increased metabolism. Whether the presence of β-oxybutyric acid molecules passing through the blood stimulates the cell activity, or whether the decrease in the alkalescence of the blood produces a similar effect, we can not at present state. Whatever the effect, the body probably to a certain extent may accustom itself to this stimulus and thus react less as time goes on. The fact that there may be 55 grams or more of β-oxybutyric acid excreted per day with diabetics, with no greater increase in the metabolism above normal than the increase found with a normal individual subsisting on a carbohydrate-free diet, who had but 4 or 5 grams of β-oxybutyric acid, would imply that as the disease progressed from day to day, the body became accustomed to the specific stimulus (probably the presence of acid) and responded less and less.[1]

Clinical experience with diabetic patients suggests that an acid intoxication of moderate severity suddenly produced by the withdrawal of carbohydrates is more dangerous than a much more severe acidosis produced by a gradual withdrawal of carbohydrates. Thus the sudden withdrawal of carbohydrates from diabetic patients upon entrance to hospitals may result in the acute onset of coma. It is often a surprise to find that in the urines of such patients the quantity of acid is so small. In contrast, cases of severe diabetes subjected to marked restriction of carbohydrates for a long period may present an acidosis of severe degree amounting to even 50 grams of β-oxybutyric acid daily, and yet show no inconvenience therefrom. In these cases the acidosis apparently greatly exceeds for weeks at a time the acidosis of the former group of cases.

[1]Rolly (*loc. cit.*), noting that the high oxygen consumption observed when patients first came to the hospital was frequently lowered by dietetic treatment, infers that this can not be explained alone by the reduction in protein ingestion, but that the previous high oxygen consumption must be due to improper diet, exercise, consumption of food, or other causes as yet unknown.

Leimdörfer (*loc. cit.*) maintains that the increased metabolism of severe diabetes is caused for the greater part by an increase in the intermediary metabolic processes, such as the formation of sugar and acetone bodies from protein and fat. A small part is due to the increased work of respiration.

As the page proof of this publication leaves our hands, we note that Grafe and Wolf (Deutsch. Archiv f. klin. Med., 1912, **107**, p. 227) probably have evidence in regard to the increased metabolism in severe diabetes as a later communication is promised.

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